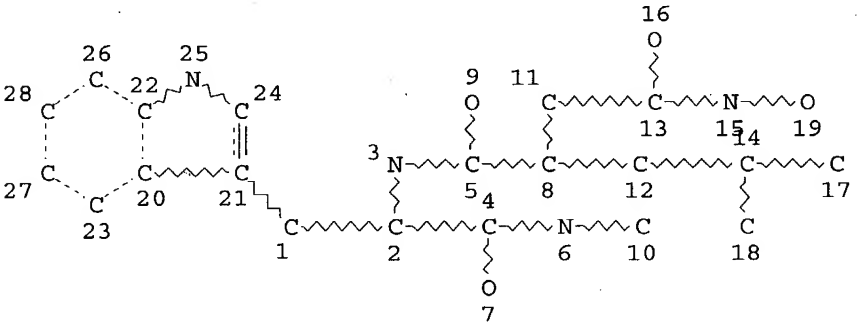
=> b hcaplus
FILE 'HCAPLUS' ENTERED AT 11:08:21 ON 04 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 4 May 2004 VOL 140 ISS 19
FILE LAST UPDATED: 3 May 2004 (20040503/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

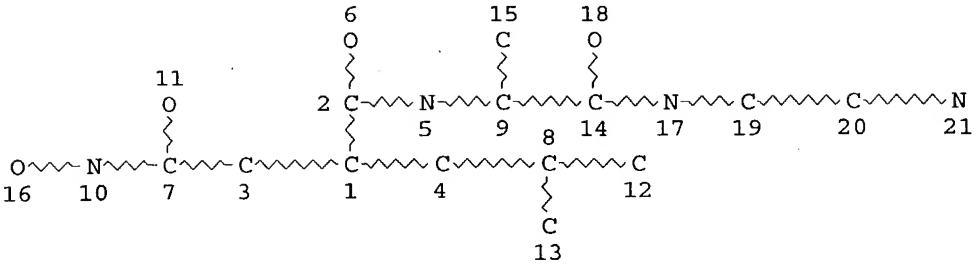
=> d que l28
L13 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L15 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

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L17          120 SEA FILE=REGISTRY SSS FUL L13
L18          178 SEA FILE=REGISTRY SSS FUL L15
L19          142 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 OR L18
L20           63 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND P/DT
L22        18281 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (ANGIOGEN?/OBI OR NEOVASC?/OBI
                 )
L24        11534 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANGIOGENESIS+NT/CT
L25         4573 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANGIOGENESIS INHIBITORS/CT
L26        14625 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 OR L25
L27        18281 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 OR L26
L28            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND L20


=> b medline
FILE 'MEDLINE' ENTERED AT 11:08:40 ON 04 MAY 2004

 FILE LAST UPDATED: 1 MAY 2004 (20040501/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l31
L29        12490 SEA FILE=MEDLINE ABB=ON  PLU=ON  "NEOVASCULARIZATION, PATHOLOGI
                 C"/CT
L30           94 SEA FILE=MEDLINE ABB=ON  PLU=ON  METALLOPROTEASES/CT
L31            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L30 AND L29


=> b embase
FILE 'EMBASE' ENTERED AT 11:09:00 ON 04 MAY 2004
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FILE COVERS 1974 TO 29 Apr 2004 (20040429/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l44

L32 7953 SEA FILE=EMBASE ABB=ON PLU=ON "NEOVASCULARIZATION (PATHOLOGY)"/CT OR "TUMOR VASCULARIZATION"/CT

L41 120 SEA FILE=REGISTRY ABB=ON PLU=ON (142880-36-2/BI OR 142880-37-3/BI OR 142880-38-4/BI OR 142880-40-8/BI OR 142880-46-4/BI OR 142880-50-0/BI OR 142880-53-3/BI OR 142880-57-7/BI OR 142880-58-8/BI OR 142880-59-9/BI OR 142880-60-2/BI OR 142880-62-4/BI OR 142880-75-9/BI OR 142902-71-4/BI OR 143457-41-4/BI OR 143479-06-5/BI OR 143985-20-0/BI OR 143985-22-2/BI OR 143985-24-4/BI OR 143985-25-5/BI OR 143985-51-7/BI OR 144007-85-2/BI OR 144007-86-3/BI OR 144007-87-4/BI OR 144007-88-5/BI OR 144007-89-6/BI OR 144022-77-5/BI OR 144022-78-6/BI OR 144069-98-7/BI OR 148811-73-8/BI OR 148811-74-9/BI OR 148811-82-9/BI OR 148811-83-0/BI OR 148811-84-1/BI OR 148811-85-2/BI OR 153465-42-0/BI OR 153465-46-4/BI OR 159686-32-5/BI OR 159686-33-6/BI OR 159686-34-7/BI OR 161177-32-8/BI OR 161177-33-9/BI OR 161177-34-0/BI OR 161177-35-1/BI OR 161177-36-2/BI OR 161177-37-3/BI OR 161177-38-4/BI OR 161177-39-5/BI OR 161696-77-1/BI OR 161696-81-7/BI OR 162550-05-2/BI OR 167224-02-4/BI OR 171347-79-8/BI OR 171347-80-1/BI OR 171347-81-2/BI OR 171347-82-3/BI OR 171347-83-4/BI OR 171347-84-5/BI OR 171347-85-6/BI OR 171347-98-1/BI OR 171348-01-9/BI OR 171348-02-0/BI OR 171348-03-1/BI OR 171348-04-2/BI OR 185334-73-0/BI OR 185334-74-1/BI OR 200866-13-3/BI OR 200866-14-4/BI OR 200866-22-4/BI OR 200866-23-5/BI OR 200866-24-6/BI OR 200866-25-7/BI OR 200866-26-8/BI OR 200866-27-9/BI OR 200866-28-0/BI OR 200866-29-1/BI OR 200866-30-4/BI OR 200866-31-5/BI OR 200866-32-6/BI OR 200866-33-7/BI OR 200866-36-0/BI OR 200866-56-4/BI OR 200866-57-5/BI OR 200866-81-5/BI OR 200866-86-0/BI OR 200866-87-1/BI OR 200959-08-6/BI OR 205807-08-5/BI OR 205807-28-9/BI OR 215310-95-5/BI OR 221622-65-7/BI OR 221622-69-1/BI OR 221622-71-5/BI OR 221622-75-9/BI OR 221622-77-1/BI OR 221622-82-8/BI OR 221622-83-9/BI OR 221622-86-2/BI OR 221622-94-2/BI OR 221

L42 178 SEA FILE=REGISTRY ABB=ON PLU=ON (106314-87-8/BI OR 112105-58-5/BI OR 112105-59-6/BI OR 112105-60-9/BI OR 112105-61-0/BI OR 112105-63-2/BI OR 112105-86-9/BI OR 112105-87-0/BI OR 112105-88-1/BI OR 112105-89-2/BI OR 113614-62-3/BI OR 113614-66-7/BI OR 113614-70-3/BI OR 113614-71-4/BI OR 130128-39-1/BI OR 135775-00-7/BI OR 143457-40-3/BI OR 143457-41-4/BI OR 143457-42-5/BI OR 143457-43-6/BI OR 143457-44-7/BI OR 143479-06-5/BI OR 148745-00-0/BI OR 148745-09-9/BI OR 148745-35-1/BI OR 148745-36-2/BI OR 148745-37-3/BI OR 148745-38-4/BI OR 148745-39-5/BI OR 148745-40-8/BI OR 148745-43-1/BI OR 148811-56-7/BI OR 148811-66-9/BI OR 148811-67-0/BI OR 148811-68-1/BI OR 148811-73-8/BI OR 148811-74-9/BI OR 148811-75-0/BI OR 148811-76-1/BI OR 148811-77-2/BI OR 148811-78-3/BI OR 148811-79-4/BI OR 148811-80-7/BI OR 148811-81-8/BI OR 148811-82-9/BI OR 148811-83-0/BI OR 148811-84-1/BI OR 148811-85-2/BI OR 148811-86-3/BI OR 148811-88-5/BI OR 148812-14-0/BI OR 155832-42-1/BI OR 155865-40-0/BI OR 161177-39-5/BI OR 163847-77-6/BI OR 163847-78-7/BI OR 163847-82-3/BI OR 163847-83-4/BI OR 163847-84-5/BI OR 163847-87-8/BI OR 163847-88-9/BI OR

163847-98-1/BI OR 163848-00-8/BI OR 163848-03-1/BI OR 163848-05
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177162-67-3/BI OR 177162-72-0/BI OR 177162-73-1/BI OR 177

L43 288 SEA FILE=REGISTRY ABB=ON PLU=ON L41 OR L42
L44 12 SEA FILE=EMBASE ABB=ON PLU=ON L43 AND L32

=> b biosis
FILE 'BIOSIS' ENTERED AT 11:09:09 ON 04 MAY 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 28 April 2004 (20040428/ED)

FILE RELOADED: 19 October 2003.

=> d que l58
L41 120 SEA FILE=REGISTRY ABB=ON PLU=ON (142880-36-2/BI OR 142880-37-
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148811-84-1/BI OR 148811-85-2/BI OR 153465-42-0/BI OR 153465-46
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L42 178 SEA FILE=REGISTRY ABB=ON PLU=ON (106314-87-8/BI OR 112105-58-
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                -7/BI OR 163958-69-8/BI OR 163958-70-1/BI OR 163958-71-2/BI OR
                163958-73-4/BI OR 163958-74-5/BI OR 163958-76-7/BI OR 163958-78
                -9/BI OR 163958-80-3/BI OR 163958-82-5/BI OR 163958-85-8/BI OR
                166811-02-5/BI OR 166811-03-6/BI OR 166811-05-8/BI OR 166811-10
                -5/BI OR 166811-11-6/BI OR 166811-17-2/BI OR 166811-24-1/BI OR
                168399-06-2/BI OR 171235-71-5/BI OR 176181-41-2/BI OR 176776-68
                -4/BI OR 177162-56-0/BI OR 177162-59-3/BI OR 177162-62-8/BI OR
                177162-67-3/BI OR 177162-72-0/BI OR 177162-73-1/BI OR 177
L43          288 SEA FILE=REGISTRY ABB=ON  PLU=ON  L41 OR L42
L48           42 SEA FILE=BIOSIS ABB=ON  PLU=ON  L43
L51         8015 SEA FILE=BIOSIS ABB=ON  PLU=ON  (METALLOPROT?)(2A)(INHIB? OR
                 BLOCK? OR ANTAG?)
L52           28 SEA FILE=BIOSIS ABB=ON  PLU=ON  L51 AND L48
L58            4 SEA FILE=BIOSIS ABB=ON  PLU=ON  L52 AND (?CANC? OR ?TUMOR? OR
                 ?TUMOUR?)


=> dup rem l58 l31 l44 l28
FILE 'BIOSIS' ENTERED AT 11:09:48 ON 04 MAY 2004
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FILE 'MEDLINE' ENTERED AT 11:09:48 ON 04 MAY 2004

FILE 'EMBASE' ENTERED AT 11:09:48 ON 04 MAY 2004
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PROCESSING COMPLETED FOR L58
PROCESSING COMPLETED FOR L31
PROCESSING COMPLETED FOR L44
PROCESSING COMPLETED FOR L28
L59           25 DUP REM L58 L31 L44 L28 (0 DUPLICATES REMOVED)

=> d all l59 1-25

L59  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:252305  HCAPLUS
```

DN 140:281409
ED Entered STN: 26 Mar 2004
TI Inhibition or activation of ADAM9 and ADAM15 for treatment of vascularization-related disease and wound healing
IN Blobel, Carl P.; Horiuchi, Keisuke; Weskamp, Gisela; Preissner, Klaus
PA Sloan-Kettering Institute for Cancer Research, USA; University of Mannheim/heidelberg; Justus-Liebig-Universitaet Giessen; Hammes, Hans-Peter
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K
CC 1-12 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004024089	A2	20040325	WO 2003-US28751	20030911

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-409858P P 20020911
AB Inhibition of neovascularization is achieved by exposing a tissue susceptible to neovascularization to a therapeutic agent effective to inhibit ADAM9 and/or ADAM15. The therapeutic agent may be, for example, an antibody, a small mol. therapeutic, an antisense or RNAi therapeutic, or an agent for introducing targeted mutations in the genetic sequence for ADAM9 and/or ADAM15. Thus, an individual suffering from a condition associated with pathol. neovascularization is treated by administration of a therapeutic agent effective to inhibit an ADAM9 or ADAM15. Activation of ADAM9 or ADAM15 can be used for promotion of neovascularization, for example to facilitate wound healing, perfusion or circulation. In this case, the therapeutic agent used is one which enhances the active amount of ADAM9 and/or ADAM15. Inhibition or activation of ADAM9 and/or ADAM15 in accordance with the methods of the invention provides an attractive alternative to targeting of other ADAM species, such as ADAM10, because neither ADAM9 nor ADAM15 appears to be essential for development or maintenance. Thus, side effects are minimized. The growth of B16F10 melanoma tumors was reduced in ADAM9-/- and ADAM15-/- mice compared to wild-type mice.
ST ADAM9 ADAM15 vascularization disease treatment wound healing; pathol **neovascularization** treatment ADAM9 ADAM15 inhibitor; **neovascularization** promotion ADAM9 ADAM15 activation; melanoma inhibitor ADAM9 ADAM15
IT **Angiogenesis inhibitors**
Animal tissue
Antitumor agents
Human
Wound healing
Wound healing promoters
(ADAM9 and ADAM15 inhibition or activation for treatment of

vascularization-related disease and wound healing)

IT Melanoma
(ADAM9 and ADAM15 knockout mice with reduction in growth of; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Drug targets
(ADAM9 and ADAM15; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Hydroxamic acids
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADAM9 or ADAM15 inhibitors; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Circulation
Perfusion
(activation of ADAM9 and ADAM15 to facilitate; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Disease, animal
(associated with pathol. **neovascularization**, treatment of; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for ADAM9 and ADAM15; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Antibodies
Antisense nucleic acids
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibiting ADAM9 or ADAM15; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interference inhibiting ADAM9 or ADAM15; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT **Angiogenesis**
(**neovascularization**, retinal, ADAM9 and ADAM15 knockout mice in relation to; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT **Angiogenesis**
(**neovascularization**; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT **Eye, disease**
(**retina, neovascularization**, ADAM9 and ADAM15 knockout mice in relation to; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Molecules
(small, inhibiting ADAM9 or ADAM15; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT Mutation
(targeted, in ADAM9 and ADAM15; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)

IT 193099-10-4, ADAM15 674383-80-3
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,

unclassified); BIOL (Biological study)
(ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)
IT 252565-22-3
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)
IT 130370-60-4, Batimastat **143457-40-3**, TAPI 154039-60-8, Marimastat 169799-04-6, CGS 27023
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADAM9 or ADAM15 inhibitor; ADAM9 and ADAM15 inhibition or activation for treatment of vascularization-related disease and wound healing)
IT 674436-44-3 674436-45-4 674436-46-5 674436-48-7 674436-50-1 674436-51-2 674436-52-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; inhibition or activation of ADAM9 and ADAM15 for treatment of vascularization-related disease and wound healing)
IT 674436-47-6 674436-49-8
RL: PRP (Properties)
(unclaimed protein sequence; inhibition or activation of ADAM9 and ADAM15 for treatment of vascularization-related disease and wound healing)
IT 674773-04-7 674773-05-8
RL: PRP (Properties)
(unclaimed sequence; inhibition or activation of ADAM9 and ADAM15 for treatment of vascularization-related disease and wound healing)

L59 ANSWER 2 OF 25 MEDLINE on STN
AN 2004095036 MEDLINE
DN PubMed ID: 14985106
TI Apicidin is a histone deacetylase inhibitor with anti-invasive and anti-angiogenic potentials.
AU Kim Seong Hwan; Ahn Sanghun; Han Jeung-Whan; Lee Hyang-Woo; Lee Hoi Young; Lee Yin-Won; Kim Mi Ran; Kim Kye Won; Kim Won Bae; Hong Sungyoul
CS Department of Genetic Engineering, Faculty of Life Science and Technology, Sungkyunkwan University, Suwon 440-746, Republic of Korea.
SO Biochemical and biophysical research communications, (2004 Mar 19) 315 (4) 964-70.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040302
Last Updated on STN: 20040421
Entered Medline: 20040420
AB Apicidin has been identified as a histone deacetylase (HDAC) inhibitor. Since HDAC inhibitors are emerging as an exciting new class of potential anti-cancer agents, in the present study, we have examined the inhibitory effect of apicidin on cancer invasion and angiogenesis. Apicidin induced di- and tri-acetylated forms of histone H4 and the morphological alteration in v-ras-transformed mouse fibroblast NIH3T3 cells. Apicidin dramatically inhibited the invasion of v-ras-NIH3T3 and human melanoma A2058 cells and it could be associated with its ability to regulate the activities of matrix metalloproteinases. Interestingly, apicidin strongly

inhibited the formation of new vessels on chorioallantoic membrane and the tube formation of ECV304 human vascular endothelial cells. This is the first report to show the anti-angiogenic potential of apicidin and it could be developed as a new type of anti-cancer drug.

CT Check Tags: Human; Support, Non-U.S. Gov't
Allantois: DE, drug effects
*Angiogenesis Inhibitors: PD, pharmacology
Animals
*Antineoplastic Agents: PD, pharmacology
Cell Line, Transformed: DE, drug effects
Cell Line, Transformed: ME, metabolism
Cell Line, Tumor
Chick Embryo
Chorion: DE, drug effects
*Enzyme Inhibitors: PD, pharmacology
Gelatin
Genes, ras: GE, genetics
*Histone Deacetylases: AI, antagonists & inhibitors
Metalloproteases: ME, metabolism
Mice
NIH 3T3 Cells
Neoplasm Invasiveness
Neovascularization, Pathologic: ME, metabolism
*Peptides, Cyclic: PD, pharmacology

RN 9000-70-8 (Gelatin)

CN 0 (Angiogenesis Inhibitors); 0 (Antineoplastic Agents); 0 (Enzyme Inhibitors); 0 (Peptides, Cyclic); 0 (apicidin); EC 3.4.- (Metalloproteases); EC 3.5.1.- (Histone Deacetylases)

L59 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

AN 2004:192567 BIOSIS

DN PREV200400180479

TI Human meprin alpha and beta homo-oligomers: Cleavage of basement membrane proteins and sensitivity to **metalloprotease inhibitors**

AU Kruse, Markus-N.; Becker, Christoph; Lottaz, Daniel; Koehler, Danny; Yiallouros, Irene; Krell, Hans-Willi; Sterchi, Erwin E.; Stoecker, Walter [Reprint Author]

CS Institute of Zoophysiology, University of Muenster, Hindenburgplatz 55, D-48143, Muenster, Germany
wst@uni-muenster.de

SO Biochemical Journal, (1 March 2004) Vol. 378, No. 2, pp. 383-389. print. ISSN: 0264-6021.

DT Article

LA English

ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

AB Meprin is a zinc endopeptidase of the astacin family, which is expressed as a membrane-bound or secreted protein in mammalian epithelial cells, in intestinal leucocytes and in certain **cancer** cells. There are two types of meprin subunits, alpha and beta, which form disulphide-bonded homo- and hetero-oligomers. Here we report on the cleavage of matrix proteins by hmeprin (human meprin) alpha and beta homo-oligomers, and on the interactions of these enzymes with inhibitors. Despite their completely different cleavage specificities, both hmeprin alpha and beta are able to hydrolyse basement membrane components such as collagen IV, nidogen-1 and fibronectin. However, they are inactive against intact collagen I. Hence the matrix-cleaving activity of hmeprin resembles that of gelatinases rather than collagenases. Hmeprin is inhibited by

hydroxamic acid derivatives such as batimastat, galardin and Pro-Leu-Gly-hydroxamate, by TAPI-0 (**tumour** necrosis factor alpha protease inhibitor-0) and TAPI-2, and by thiol-based compounds such as captopril. Therapeutic targets for these inhibitors are MMPs (matrix metalloproteases), TACE (**tumour** necrosis factor alpha-converting enzyme) and angiotensin-converting enzyme respectively. The most effective inhibitor of hmeprin alpha in the present study was the naturally occurring hydroxamate actinonin (Ki=20 nM). The marked variance in the cleavage specificities of hmeprin alpha and beta is reflected by their interaction with the TACE inhibitor Ro 32-7315, whose affinity for the beta subunit (IC50=1.6 mM) is weaker by three orders of magnitude than that for the alpha subunit (Ki=1.6 muM). MMP inhibitors such as the pyrimidine-2,4,6-trione derivative Ro 28-2653 that are more specific for gelatinases do not bind to hmeprin, presumably due to the subtle differences in the mode of zinc binding and active-site structure between the astacins and the MMPs.

CC Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics)

IT Parts, Structures, & Systems of Organisms
basement membrane

IT Chemicals & Biochemicals
Ro 28-2653: pyrimidine-2,4,6-trione derivative; angiotensin-converting enzyme; astacin [EC 3.4.24.21]; batimastat: hydroxamic acid derivative; captopril; collagen IV; fibronectin; galardin: hydroxamic acid derivative; matrix metalloprotease [MMP]; meprin alpha; meprin beta; nidogen-1; prolyl-leucyl-glycyl-hydroxamate: hydroxamic acid derivative; **tumor** necrosis factor alpha protease inhibitor-0; **tumor** necrosis factor alpha protease inhibitor-2 [TAPI-2]; **tumor** necrosis factor alpha-converting enzyme [TACE]

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 261956-22-3 (Ro 28-2653)
9015-82-1 (angiotensin-converting enzyme)
143179-21-9 (astacin)
143179-21-9 (EC 3.4.24.21)
130370-60-4 (batimastat)
62571-86-2 (captopril)
142880-36-2 (galardin)
141907-41-7 (matrix metalloprotease)
141907-41-7 (MMP)
221147-98-4 (**tumor** necrosis factor alpha protease inhibitor-2)
221147-98-4 (TAPI-2)
151769-16-3 (**tumor** necrosis factor alpha-converting enzyme)
151769-16-3 (TACE)

L59 ANSWER 4 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2004026574 EMBASE
TI The urokinase plasminogen activator system: Role in malignancy.
AU Duffy M.J.
CS M.J. Duffy, Department of Nuclear Medicine, St. Vincent's University

Hospital, Elm Park, Dublin 4, Ireland. Michael.J.Duffy@ucd.ie
SO Current Pharmaceutical Design, (2004) 10/1 (39-49).
Refs: 123
ISSN: 1381-6128 CODEN: CPDEFP
CY Netherlands
DT Journal; General Review
FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA English
SL English
AB The urokinase plasminogen activator (uPA) system consists of the serine protease uPA, its glycolipid-anchored receptor, uPAR and its 2 serpin inhibitors, plasminogen activator inhibitor-1 (PAI-1) and plasminogen activator inhibitor-2 (PAI-2). Recent findings suggest that the uPA system is causally involved at multiple steps in cancer progression. In particular, uPA has been implicated in remodelling of the extracellular matrix, enhancing both cell proliferation and migration and modulating cell adhesion. Consistent with its role in cancer progression, multiple groups have shown that high levels of uPA in primary breast cancers are independently associated with adverse outcome. Paradoxically, high levels of PAI-1 also correlate with poor prognosis in patients with breast cancer. The prognostic value of uPA/PAI-1 in axillary node-negative breast cancer patients was recently validated using both a prospective randomised trial and a pooled analysis, i.e., in 2 different Level 1 Evidence studies. Assay of uPA and PAM may thus help identify low risk node-negative patients for whom adjuvant chemotherapy is unnecessary. Finally, preclinical studies show that either inhibition of uPA catalytic activity or prevention of uPA binding to its receptor reduces tumor growth, angiogenesis and metastasis.
CT Medical Descriptors:
carcinogenesis
extracellular matrix
cell proliferation
cell migration
cell adhesion
breast cancer: DT, drug therapy
breast cancer: ET, etiology
correlation analysis
prognosis
axillary lymph node
lymph node metastasis
risk assessment
cancer risk
cancer adjuvant therapy
drug screening
enzyme activity
enzyme inhibition
receptor binding
cancer inhibition
tumor vascularization
metastasis
receptor blocking
drug targeting
drug synthesis
drug potency
adenovirus vector

ovary cancer: DT, drug therapy
advanced cancer: DT, drug therapy
side effect: SI, side effect
human
nonhuman
clinical trial
review
priority journal
Drug Descriptors:
*urokinase
serine proteinase: EC, endogenous compound
glycolipid: EC, endogenous compound
urokinase receptor: EC, endogenous compound
serine proteinase inhibitor: DV, drug development
serine proteinase inhibitor: EC, endogenous compound
plasminogen activator inhibitor 1: EC, endogenous compound
plasminogen activator inhibitor 1: PR, pharmaceutics
plasminogen activator inhibitor 1: PK, pharmacokinetics
plasminogen activator inhibitor 1: PD, pharmacology
tranexamic acid: PD, pharmacology
aprotinin: PD, pharmacology
leupeptin: PD, pharmacology
amiloride: PD, pharmacology
antineoplastic agent: DT, drug therapy
guanidine derivative: DV, drug development
guanidine derivative: PD, pharmacology
4 chlorophenylguanidine: DV, drug development
4 chlorophenylguanidine: PD, pharmacology
4 trifluoromethylphenylguanidine: DV, drug development
4 trifluoromethylphenylguanidine: PD, pharmacology
plasminogen activator inhibitor: CT, clinical trial
plasminogen activator inhibitor: DV, drug development
plasminogen activator inhibitor: DT, drug therapy
plasminogen activator inhibitor: PD, pharmacology
b 428: CB, drug combination
b 428: DV, drug development
b 428: IT, drug interaction
b 428: PD, pharmacology
b 623: DV, drug development
b 623: PD, pharmacology
wx uk1: CT, clinical trial
wx uk1: PD, pharmacology
wx 360: DV, drug development
wx 360: DT, drug therapy
wx 360: PD, pharmacology
tamoxifen: CB, drug combination
tamoxifen: IT, drug interaction
tamoxifen: PD, pharmacology
plasminogen activator inhibitor 2: EC, endogenous compound
plasminogen activator inhibitor 2: PK, pharmacokinetics
plasminogen activator inhibitor 2: PD, pharmacology
matrix metalloproteinase inhibitor: AE, adverse drug reaction
matrix metalloproteinase inhibitor: CT, clinical trial
matrix metalloproteinase inhibitor: DT, drug therapy
ilomastat: PD, pharmacology
wx 360 nle: DV, drug development
wx 360 nle: DT, drug therapy
wx 360 nle: PD, pharmacology
unclassified drug

RN (urokinase) 139639-24-0; (serine proteinase) 37259-58-8; (plasminogen activator inhibitor 1) 140208-23-7; (tranexamic acid) 1197-18-8, 701-54-2; (aprotinin) 11004-21-0, 12407-79-3, 50936-63-5, 52229-70-6, 58591-29-0, 9050-74-2, 9075-10-9, 9087-70-1; (leupeptin) 54577-99-0; (amiloride) 2016-88-8, 2609-46-3; (plasminogen activator inhibitor) 105844-41-5; (tamoxifen) 10540-29-1; (plasminogen activator inhibitor 2) 142243-03-6; (ilomastat) **142880-36-2**
CN (1) Wx uk1; B 428; B 623; Wx 360; Wx 360 nle
CO (1) Wilex (Germany)

L59 ANSWER 5 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:503212 BIOSIS
DN PREV200300498812
TI Membrane type-1 matrix metalloproteinase (MT1-MMP) binding of tissue **inhibitor** of **metalloproteinase**-2 (TIMP-2) modulates breast **cancer** cell functions through generation of intracellular signaling.
AU D'Alessio, Silvia [Reprint Author]; Pintucci, Giuseppe [Reprint Author]; Roses, Daniel F. [Reprint Author]; Berman, Russell S. [Reprint Author]; Mignatti, Paolo [Reprint Author]
CS New York University School of Medicine, New York, NY, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 1243. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Reproductive system - Physiology and biochemistry 16504
Reproductive system - Pathology 16506
Neoplasms - Pathology, clinical aspects and systemic effects 24004
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Reproductive System (Reproduction); **Tumor** Biology
IT Diseases
breast **cancer**: neoplastic disease, reproductive system disease/female
Breast Neoplasms (MeSH)
IT Chemicals & Biochemicals
Ras: expression; Ras/MAP kinase; extracellular signal-regulated kinase 1/2: expression; ilomastat: enzyme inhibitor-drug; matrix metalloproteinase-2; membrane type-1 matrix metalloproteinase: expression; tetracycline resistance promoter; tissue **inhibitor** of **metalloproteinase**-2; urokinase plasminogen activator: expression
IT Miscellaneous Descriptors
intracellular signaling
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
MCF-7 cell line (cell line): human breast **cancer** cells

Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN **142880-36-2** (ilomastat)
146480-35-5 (matrix metalloproteinase-2)
161384-17-4 (membrane type-1 matrix metalloproteinase)
124861-55-8 (tissue **inhibitor** of **metalloproteinase**-2)
9039-53-6 (urokinase plasminogen activator)
GEN human uPA gene [human urokinase plasminogen activator gene] (Hominidae)

L59 ANSWER 6 OF 25 MEDLINE on STN
AN 2003550840 MEDLINE
DN PubMed ID: 14630537
TI Intramural neovascularization and haemorrhages are major long-term effects of intravascular gamma-radiation after stenting.
AU Busseuil D; Zeller M; Cottin Y; Maingon P; Barillot I; Martin L; Allouch P; Lalande A; Vergely C; Briot F; Piard F; Wolf J E; Rochette L
CS Laboratory of Cardiovascular and Experimental Physiopathology and Pharmacology Faculty of Medicine, University of Burgundy, Dijon, France.
SO International journal of radiation biology, (2003 Oct) 79 (10) 787-92. Journal code: 8809243. ISSN: 0955-3002.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Space Life Sciences
EM 200402
ED Entered STN: 20031122
Last Updated on STN: 20040206
Entered Medline: 20040205
AB Structural changes that might influence the structural integrity of the vessel in response to intravascular brachytherapy (IVB) and stenting were examined, focus being on the importance of neovascularization in rabbit stented arteries. Stents were implanted in the infrarenal aortas of rabbits, immediately followed by gamma IVB or a sham radiation procedure, and the arteries harvested at 6 months. Labelling for von Willebrand factor showed an increase in adventitial and medial neovascularization in irradiated versus control arteries group (5.04+/-0.89 versus 1.51+/-0.23 mm(-2), respectively; p=0.004). Moreover, intramedial haemorrhages (free hemosiderin deposition) and inflammation (macrophages) were only observed in irradiated arteries. No significant change in expression of matrix metalloproteinase 1, 2 or 3 was observed between the irradiated and control group while collagen content decreased in the irradiated versus the control group (10.05%+/-1.48% versus 31.92%+/-3.12%, respectively; p<0.001). The study supports the hypothesis that IVB associated with stenting induces late deleterious effects on the medial layer, characterized by formation of intramural neovessels, haemorrhages and a decrease in collagen content.
CT Check Tags: Comparative Study; Male; Support, Non-U.S. Gov't
Animals
Aorta, Abdominal: ME, metabolism
*Aorta, Abdominal: PA, pathology
*Aorta, Abdominal: RE, radiation effects
Aorta, Abdominal: SU, surgery
*Brachytherapy: AE, adverse effects
Collagen: ME, metabolism
Coronary Restenosis: PC, prevention & control
Coronary Restenosis: RT, radiotherapy
Gamma Rays: AE, adverse effects
*Hemorrhage: ET, etiology
Hemorrhage: ME, metabolism

Hemorrhage: PA, pathology
Metalloproteases: ME, metabolism
***Neovascularization, Pathologic: ET, etiology**
Rabbits
Reference Values
*Stents: AE, adverse effects
*Vascular Diseases: ET, etiology
Vascular Diseases: ME, metabolism
Vascular Diseases: PA, pathology
RN 9007-34-5 (Collagen)
CN EC 3.4.- (Metalloproteases)

L59 ANSWER 7 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2003427556 EMBASE
TI Retinal and choroidal angiogenesis: Pathophysiology and strategies for inhibition.
AU Das A.; McGuire P.G.
CS A. Das, School of Medicine, University of New Mexico, Albuquerque, NM, United States. adas@unm.edu
SO Progress in Retinal and Eye Research, (2003) 22/6 (721-748).
Refs: 225
ISSN: 1350-9462 CODEN: PRTRES
CY United Kingdom
DT Journal; General Review
FS 012 Ophthalmology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Retinal angiogenesis and choroidal angiogenesis are major causes of vision loss, and the pathogenesis of this angiogenesis process is still uncertain. However, several key steps of the angiogenic cascade have been elucidated. In retinal angiogenesis, hypoxia is the initial stimulus that causes up regulation of growth factors, integrins and proteinases, which result in endothelial cell proliferation and migration that are critical steps in this process. Once the endothelial tube is formed from the existing blood vessels, maturation starts with recruitment of mural cell precursors and formation of the basement membrane. Normally, there is a tight balance between angiogenic factors and endogenous angiogenesis inhibitors that help to keep the angiogenic process under control. Although the steps of choroidal angiogenesis seem to be similar to those of retinal angiogenesis, there are some major differences between these two processes. Several anti-angiogenic approaches are being developed in animal models to prevent ocular angiogenesis by blocking the key steps of the angiogenic cascade. Based on these pre-clinical studies, several anti-angiogenic clinical trials are ongoing in patients with diabetic retinopathy and age-related macular degeneration. This review discusses the pathogenesis of retinal and choroidal angiogenesis, and alternative pharmacological approaches to inhibit angiogenesis in ocular diseases.
CT Medical Descriptors:
*retina
*choroid
*angiogenesis
pathophysiology
inhibition kinetics
visual impairment

hypoxia
upregulation
endothelium cell
cell proliferation
cell migration
blood vessel
cell maturation
precursor cell
basement membrane
experimental model
diabetic neuropathy: DT, drug therapy
retina macula degeneration: DT, drug therapy
eye disease: DT, drug therapy
neovascularization (pathology): DT, drug therapy
subretinal neovascularization: DT, drug therapy
retina neovascularization: DT, drug therapy
disease model
regulatory mechanism
protein analysis
drug mechanism
drug effect
human
clinical trial
review
priority journal
Drug Descriptors:
growth factor
integrin
angiogenic factor
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PR, pharmaceutics
angiogenesis inhibitor: PD, pharmacology
angiogenesis inhibitor: IM, intramuscular drug administration
angiogenesis inhibitor: VI, intravitreal drug administration
Tie2 receptor: DT, drug therapy
Tie2 receptor: PD, pharmacology
Tie2 receptor: IM, intramuscular drug administration
tek delta fc: DT, drug therapy
tek delta fc: PD, pharmacology
vasculotropin
basic fibroblast growth factor
somatomedin
angiopoietin
platelet derived growth factor
tumor necrosis factor alpha
dipeptidyl carboxypeptidase
nitric oxide
urokinase
matrix metalloproteinase
transforming growth factor beta
pigment epithelium derived factor
angiostatin
thrombospondin 1
tissue inhibitor of metalloproteinase
vasculotropin inhibitor: DT, drug therapy
vasculotropin inhibitor: VI, intravitreal drug administration
ruboxistaurin: CT, clinical trial
ruboxistaurin: DT, drug therapy

ruboxistaurin: PD, pharmacology
protein kinase C inhibitor: DT, drug therapy
protein kinase C inhibitor: PD, pharmacology
protein kinase C inhibitor: PO, oral drug administration
pkc 412: DT, drug therapy
pkc 412: PD, pharmacology
pkc 412: PO, oral drug administration
seglitide: DT, drug therapy
seglitide: PD, pharmacology
ilomastat: DT, drug therapy
ilomastat: PD, pharmacology
batimastat: DT, drug therapy
batimastat: PD, pharmacology
prinomastat: DT, drug therapy
prinomastat: PD, pharmacology
unindexed drug
unclassified drug
bm 94

RN (vasculotropin) 127464-60-2; (basic fibroblast growth factor) 106096-93-9; (angiopoietin) 250740-90-0; (dipeptidyl carboxypeptidase) 9015-82-1; (nitric oxide) 10102-43-9; (urokinase) 139639-24-0; (pigment epithelium derived factor) 197980-93-1; (angiostatin) 172642-30-7, 86090-08-6; (thrombospondin 1) 343987-56-4; (tissue inhibitor of metalloproteinase) 97837-28-0; (ruboxistaurin) 169939-93-9, 169939-94-0; (seglitide) 118232-51-2, 81377-02-8; (ilomastat) **142880-36-2**; (batimastat) 130370-60-4, 130464-84-5; (prinomastat) 192329-42-3, 195008-93-6

CN (1) Ag 3340; Ly 333531; Pkc 412; Mk 678; Gm 6001; Bm 94

CO (1) Agouron

L59 ANSWER 8 OF 25 EMBASE
on STN

AN 2003420167 EMBASE

TI Radiotracer-based strategies to image angiogenesis.

AU Haubner R.; Wester H.J.; Weber W.A.; Schwaiger M.

CS Dr. R. Haubner, Nuklearmedizinische Klinik, Technische Universitat Munchen, Ismaningerstr. 22, 81675 Munich, Germany. R.Haubner@lrz.tum.de

SO Quarterly Journal of Nuclear Medicine, (2003) 47/3 (189-199).
Refs: 83
ISSN: 1124-3937 CODEN: QJNMF7

CY Italy

DT Journal; General Review

FS 016 Cancer
023 Nuclear Medicine
030 Pharmacology
029 Clinical Biochemistry
037 Drug Literature Index

LA English

SL English

AB Tumour-induced angiogenesis plays an important role in tumour progression. Great efforts are made to develop therapeutic strategies to interfere with this process resulting in the starvation of the tumour. However, strategies to monitor conventional therapies seems to be inappropriate to control these approaches. Thus, there is a keen interest in developing methods supplying information about the corresponding therapeutical effects. Several radiotracer-based approaches focused on different targets in the angiogenic process are currently investigated. One class of tracers is based on matrix metalloproteinases inhibitors. These compounds show promising results in in vitro assays. However, initial data from in vivo studies using murine tumour models could not confirm successful

non-invasive monitoring of MMP activity yet. Another strategy uses a radiolabelled single chain fragment against the ED-B domain of fibronectin, an extracellular matrix protein. Promising results demonstrated selective accumulation of the tracer in the tumour vasculature of a murine tumour model. Most of the studies are concentrated on the development of radiolabelled antagonists of the integrin α(v)β(3). This heterodimeric transmembrane glycoprotein is involved in the migration of activated endothelial cells during formation of new vessels. Different compounds have been labelled with (18)F, (111)In, (99m)Tc, (90)Y and several iodine isotops. In in vitro assays most of them revealed high α(v)β(3) affinity and selectivity. Moreover, in different murine tumour models successful non-invasive determination of α(v)β(3) expression has been shown. Some of these approaches indicate that tumour-induced angiogenesis can be monitored in animal studies. Nevertheless, translation of these approaches into clinical settings allowing visualisation of tumour-induced angiogenesis in patients needs still to be demonstrated.

CT Medical Descriptors:
*angiogenesis
*isotope labeling
*cancer: DT, drug therapy
human
clinical trial
nonhuman
tumor
tumor growth
treatment planning
drug classification
drug targeting
in vitro study
in vivo study
disease model
enzyme activity
non invasive measurement
protein domain
extracellular matrix
drug accumulation
tumor vascularization
protein function
endothelium cell
cell migration
cell activation
binding affinity
drug selectivity
protein determination
protein expression
cancer research
drug mechanism
apoptosis
diagnostic imaging
drug receptor binding
drug protein binding
drug structure
drug liver level
structure activity relation
combinatorial chemistry
review
Drug Descriptors:
*tracer: PK, pharmacokinetics

*tracer: CR, drug concentration
*tracer: CM, drug comparison
*tracer: PD, pharmacology
matrix metalloproteinase inhibitor: PD, pharmacology
matrix metalloproteinase inhibitor: CM, drug comparison
matrix metalloproteinase inhibitor: PK, pharmacokinetics
single chain fragment variable antibody: PD, pharmacology
fibronectin: EC, endogenous compound
matrix protein: EC, endogenous compound
protein inhibitor: PD, pharmacology
alphavbeta3 integrin antagonist: PD, pharmacology
alphavbeta3 integrin antagonist: CM, drug comparison
glycoprotein: EC, endogenous compound
gluco arginylglycylaspartic acid i 125: CR, drug concentration
gluco arginylglycylaspartic acid i 125: PK, pharmacokinetics
gluco arginylglycylaspartic acid i 125: CM, drug comparison
galacto arginylglycylaspartic acid f 18: CR, drug concentration
galacto arginylglycylaspartic acid f 18: PK, pharmacokinetics
galacto arginylglycylaspartic acid f 18: CM, drug comparison
pentetate arginylglycylaspartic acid in 111: PK, pharmacokinetics
pentetate arginylglycylaspartic acid in 111: CM, drug comparison
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
arginylglycylaspartic acid y 90: PK, pharmacokinetics
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
arginylglycylaspartic acid y 90: CM, drug comparison
cyclo(arginylglycylaspartyl dextro phenylalanyltyrosine) i 125: PD, pharmacology
cyclo(arginylglycylaspartyl dextro phenylalanyltyrosine) i 125: PK, pharmacokinetics
cyclo(arginylglycylaspartyl dextro phenylalanyltyrosine) i 125: CR, drug concentration
cyclo(arginylglycylaspartyl dextro phenylalanyltyrosine) i 125: CM, drug comparison
integrin: EC, endogenous compound
vitronectin receptor: EC, endogenous compound
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT, drug therapy
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
marimastat: DT, drug therapy
marimastat: CT, clinical trial
marimastat: PD, pharmacology
tanomastat: DT, drug therapy
tanomastat: CT, clinical trial
tanomastat: PD, pharmacology
cgs 27023a: DT, drug therapy
cgs 27023a: CT, clinical trial
cgs 27023a: PD, pharmacology
cgs 27023a: AN, drug analysis
cilengitide: PD, pharmacology
monoclonal antibody 1m 609: PD, pharmacology

angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: PD, pharmacology
endostatin: DT, drug therapy
endostatin: CT, clinical trial
endostatin: PD, pharmacology
angiostatin: DT, drug therapy
angiostatin: CT, clinical trial
angiostatin: PD, pharmacology
cysteinylthreonylthreonylhistidyltryptophylglycylphenylalanylthreonylleu
c ylcysteine: PD, pharmacology
cysteinylthreonylthreonylhistidyltryptophylglycylphenylalanylthreonylleu
c ylcysteine: CM, drug comparison
ilomastat: PD, pharmacology
ilomastat: CM, drug comparison
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
cysteinylthreonylthreonylhistidyltryptophylglycylphenylalanylthreonylleucy
lcyste ine: PD, pharmacology
1,4,7,10 tetraazacyclododecane 1,4,7,10 tetraacetic acid
cysteinylthreonylthreonylhistidyltryptophylglycylphenylalanylthreonylleucy
lcyste ine: CM, drug comparison
cyclo(arginylglycylaspartyl dextro tyrosylvaline) i 125: PD, pharmacology
cyclo(arginylglycylaspartyl dextro tyrosylvaline) i 125: PK,
pharmacokinetics
cyclo(arginylglycylaspartyl dextro tyrosylvaline) i 125: CR, drug
concentration
cyclo(arginylglycylaspartyl dextro tyrosylvaline) i 125: CM, drug
comparison
unindexed drug
unclassified drug

RN (single chain fragment variable antibody) 334577-34-3, 334577-38-7; (fibronectin) 86088-83-7; (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (marimastat) 154039-60-8; (tanomastat) 179545-76-7, 179545-77-8; (cgs 27023a) 169799-04-6; (cilengitide) 188968-51-6; (endostatin) 187888-07-9; (angiostatin) 172642-30-7, 86090-08-6; (ilomastat) **142880-36-2**

CN (1) Cgs 27023a; Su 5416; Su 6668; Marimastat; Bay 129566; Endostatin; Emd 121974; Vitaxin; Angiostatin; Ilomastat

CO (1) Novartis; Bristol Myers Squibb

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AN 2003437787 EMBASE

TI A novel RGD antagonist that targets both αvβ3 and α5β1 induces apoptosis of angiogenic endothelial cells on type I collagen.

AU Meerovitch K.; Bergeron F.; Leblond L.; Grouix B.; Poirier C.; Bubenik M.; Chan L.; Gourdeau H.; Bowlin T.; Attardo G.

CS K. Meerovitch, Phytobiotec Inc., 525 boul. des Prairies, Laval, Que. H7V 1B7, Canada. karen.meerovitch@phytobiotech.com

SO Vascular Pharmacology, (2003) 40/2 (77-89).
Refs: 47
ISSN: 1537-1891 CODEN: VPAHAJ

CY United States

DT Journal; Article

FS 016 Cancer
025 Hematology
030 Pharmacology

037 Drug Literature Index
LA English
SL English
AB Integrin-mediated cell adhesion is necessary for endothelial cell proliferation and apoptosis, which is a major determinant in tumor-induced angiogenesis. In this study, we compared two novel, structurally similar, Arg-Gly-Asp (RGD) peptidomimetic compounds having different integrin selectivities, for their inhibition of endothelial cell proliferation and induction of apoptosis on functionally relevant extracellular matrices (ECM) for angiogenesis. BCH-14661 was specific for integrin αvβ3, whereas BCH-15046 nonselectively antagonized integrins αvβ3, αvβ5, and α5β1. Both compounds were potent inducers of endothelial cell apoptosis when plated on RGD-dependent ECM (vitronectin, VN), which was dependent on the ability to induce cell detachment. However, with endothelial cells plated on RGD-independent ECM (type I collagen, COL), only BCH-15046 was able to significantly prevent growth and induce apoptosis. This effect was not dependent on the induction of detachment. Experiments using the matrix metalloproteinase (MMP) inhibitor GM 6001 revealed that cleavage of COL was not required for the ability of BCH-15046 to induce apoptosis. However, the inhibition of growth factor-stimulated endothelial cell proliferation, required MMPs, and correlated with BCH-15046s' potent inhibition of endothelial cell attachment to denatured collagen. Antibody inhibition experiments showed that adhesion to denatured collagen required integrins αvβ3 and β1, but not αvβ5. In addition, BCH-15046 exerted a significant inhibition of VEGF-stimulated angiogenesis in the chick chorioallontoic membrane in vivo. These results suggest that integrin antagonism of both αvβ3 and α5β1 are important for MMP-independent induction of apoptosis on COL and MMP-dependent inhibition of endothelial cell-denatured collagen interactions required for proliferation.
CT Medical Descriptors:
*apoptosis
*endothelium cell
*angiogenesis
*antineoplastic activity
cell proliferation
extracellular matrix
cell growth
cell division
experiment
chorioallantois
denaturation
structure analysis
correlation analysis
cell culture
protein expression
protein analysis
cell adhesion
statistical analysis
IC 50
fluorescence
culture medium
anoikis
tumor vascularization
drug targeting
drug specificity
drug mechanism
concentration response

human
nonhuman
human cell
animal cell
article
priority journal
Drug Descriptors:
*collagen type 1
*bch 14661: CM, drug comparison
*bch 14661: DO, drug dose
*bch 14661: PD, pharmacology
*bch 15046: CM, drug comparison
*bch 15046: DO, drug dose
*bch 15046: PD, pharmacology
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DO, drug dose
*antineoplastic agent: PD, pharmacology
*angiogenesis inhibitor: DO, drug dose
*angiogenesis inhibitor: PD, pharmacology
alpha5 integrin: EC, endogenous compound
vitronectin
metalloproteinase inhibitor
growth factor: PD, pharmacology
antibody: PD, pharmacology
vasculotropin antibody
vasculotropin
protein subunit: EC, endogenous compound
echistatin: CM, drug comparison
echistatin: DO, drug dose
echistatin: PD, pharmacology
monoclonal antibody
ilomastat: PD, pharmacology
unclassified drug
RN (vasculotropin) 127464-60-2; (echistatin) 118337-11-4; (ilomastat) **142880-36-2**
CN (1) Gm 6001; Bch 14661; Bch 15046
CO (1) Calbiochem (United States)

L59 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:521462 HCAPLUS
DN 137:88442
ED Entered STN: 12 Jul 2002
TI Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
IN Shanahan-Pendergast, Elisabeth
PA Ire.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC A61K031-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 10, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002053138	A2	20020711	WO 2002-IE1	20020102
	WO 2002053138	A3	20020919		

W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD,

UA, UG, US, VN, YU, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG
EP 1351678 A2 20031015 EP 2002-727007 20020102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI IE 2001-2 A 20010102
WO 2002-IE1 W 20020102
OS MARPAT 137:88442
AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immundysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.
ST neoplastic lesion treatment incensole furanogermacren compd; antitumor incensole furanogermacren; antimicrobial incensole furanogermacren
IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, immunomodulator based on, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
Lymphoma
(B-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BCR-ABL, antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, disease
(Crohn's, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Canarypox virus
(IL-2 of, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT GTPase-activating protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RasGAP, inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Sdi 1, mimetics, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Skin, neoplasm
(Sezary syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
Lymphoma
(T-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Transcription factors

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WT1 (Wilms' tumor suppressor 1), therapy based on; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Keratosis
(actinic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Leukemia
(acute; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lung, neoplasm
(adenocarcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Melanoma
(amelanotic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Urokinase-type plasminogen activator receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-dorsalizing morphogenetic protein-1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Androgens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiandrogens, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Estrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Antitumor agents
(antineoplastons, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Nutrients
(antinutrients, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug resistance
(antitumor; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lung, disease
(aspergillosis, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Infection
(bacterial, intracellular or extracellular, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Raf, antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Candida
(candidiasis from, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Prostate gland, neoplasm
(carcinoma, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Ovary, neoplasm
Stomach, neoplasm
(carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Mycobacterium
(cell wall sk and monophosphoryl lipid A, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Diterpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cembranoid, alcs.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Diterpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cembranoid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nervous system, disease
(central, precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nervous system, neoplasm
(central; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Uterus, disease
(cervix, dysplasia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Uterus, neoplasm
(cervix; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Porphyrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins, benzo-, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Porphyrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(chronic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-, enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, neoplasm
(colon, carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, neoplasm

(colon, polyp; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine
(colon, precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, neoplasm
(colon; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with pyridoxylated Hb; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Quinones
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclopentanthraquinones, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Immunity
(disorder, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Stem cell
(division inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug targeting to HIV infected cells using; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Bronchi, disease
Prostate gland, disease
(dysplasia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Skin, neoplasm
(dysplastic nevus syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Dendritic cell
(enhancement of endogenous precursor; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Heat-shock proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancement of endogenous; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(enteric-coated; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(enteric; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Escherichia coli

(enterohemorrhagic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Escherichia coli
(enteroinvasive, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Escherichia coli
(enteropathogenic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Escherichia coli
(enterotoxigenic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lung, neoplasm
(epidermoid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Gene therapy
(erythrocyte, vector system, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for apoptosis, modulators of, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Multidrug resistance
(gene inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Apoptosis
(gene modulators or regulators, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Erythrocyte
(gene therapy vector system, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env, drug targeting to HIV infected cells using antibodies to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp160env, drug targeting to HIV infected cells using antibodies to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Leukemia
(hairy-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulant, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Chemotherapy

Parasiticides
Radiotherapy
Surgery
(in combination with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Adrenal gland, neoplasm
Anti-AIDS agents
Anti-infective agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antidiarrheals
Antitumor agents
Bladder, neoplasm
Brain, neoplasm
Burn
Drug delivery systems
Enterococcus faecalis
Hodgkin's disease
Human
Lymphoma
Mammary gland, neoplasm
Melanoma
Mouth, neoplasm
Multiple myeloma
Neoplasm
Newborn
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Sarcoma
Staphylococcus aureus
Stomach, neoplasm
Testis, neoplasm
(incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Yeast
(infection with, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Intestine, disease
(inflammatory, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Cartilage
(inhibitor derived from, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Stem cell
(inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Insulin-like growth factor I receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Translation, genetic
(inhibitors of, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Signal transduction, biological
(inhibitors or modulators, pharmaceutical formulation further

including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Macrophage migration inhibitory factor
Ras proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Insulin-like growth factor-binding proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin-like growth factor I-binding, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Parasite
(intracellular or extracellular infection with, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Gamma ray
(irradiation, treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Intestine, disease
(irritable bowel syndrome, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Digestive tract
(irritation, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Paracoccidioides
(juvenile paracoccidiomyosis, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lung, neoplasm
(large-cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Bladder, disease
Skin, disease
(lesions; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Virus
(lipid envelope, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipophilic disaccharide, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(liposomes; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lytic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Pulverization
(micronization; incensole and furanogermacrens and compds. as antitumor

and antimicrobial agents)
IT Double stranded RNA
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mismatched, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, conjugates, with liposome or carbohydrate vehicles, to tumor-associated antigen; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antibodies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, to human chorionic gonadotropin, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(monocytic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lipid A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monophosphates, and mycobacterium cell wall sk, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nerve, disease
(motor, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Gram-positive bacteria (Firmicutes)
(multi-drug resistant; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(multidrug resistance, inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(myelogenous; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(myelomonocytic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(nasal; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Hematopoietic precursor cell
(neoplasm; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nerve, neoplasm
(neuroblastoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antioxidants
(nitroxide, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lymphocyte
(null cell, leukemia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interleukin 2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of canarypox virus, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oral inducer, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(oral; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(parenterals; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antiviral agents
(pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT **Angiogenesis inhibitors**
Antivenoms
Cytotoxic agents
Immunostimulants
Mycobacterium bovis
Venoms
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antisense oligonucleotides
Estrogens
Heregulins
Hormones, animal, biological studies
Interleukins
Leukemia inhibitory factor
Oligonucleotides
Polyamines
Ribozymes
Steroids, biological studies
Taxanes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Disease, animal
(polyposis syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(poppy seed-oil, Et esters, labeled with iodine-131, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Kidney, disease
Lung, disease
Mammary gland, disease

Stomach, disease
(precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(prodrugs; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Hemoglobins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products, with pyridoxal phosphate, conjugates with polyoxyethylene, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(rectal; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Kidney, neoplasm
(renal cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Antitumor agents
(resistance to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporin, fibroblast growth factor conjugates; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(senescence-derived inhibitor 1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Oligonucleotides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sense, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Shock (circulatory collapse)
(septic, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single chain antigen binding protein, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Cell wall
(sk of mycobacteria and monophosphoryl lipid A, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Leukemia
(small cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lung, neoplasm
(small-cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Neoplasm
(solid; incensole and furanogermacrens and compds. as antitumor and

antimicrobial agents)
IT Carcinoma
(squamous cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(sublingual; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Glycosaminoglycans, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lupus erythematosus
(systemic, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Human immunodeficiency virus
(targeting to cells infected with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(thymopoietin, agonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(topical; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Stem cell factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(totipotent, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Adeno-associated virus
Balantidium
Balantidium coli
Borrelia
Campylobacter
Candida
Coronavirus
Cryptococcus (fungus)
Cryptosporidium
DNA viruses
Entamoeba
Entamoeba histolytica
Filovirus
Flavivirus
Haemophilus
Hantavirus
Human papillomavirus
Human parainfluenza virus
Human poliovirus
Influenza virus
Legionella
Leishmania
Leishmania braziliensis
Leishmania donovani
Leishmania mexicana
Leishmania tropica
Listeria
Measles virus

Mycoplasma
Papillomavirus
Pestivirus
Picornaviridae
Plasmodium berghei
Plasmodium falciparum
Plasmodium malariae
Plasmodium ovale
Plasmodium vivax
Pneumocystis
Pneumocystis carinii
Poxviridae
Pseudomonas
RNA viruses
Respiratory syncytial virus
Retroviridae
Rhinovirus
Rubivirus
Salmonella
Shigella
Staphylococcus
Streptococcus
Togaviridae
Toxoplasma
Toxoplasma gondii
Trichomonas
Trichomonas vaginalis
Trypanosoma
Trypanosoma brucei
Trypanosoma cruzi
Trypanosoma gambiense
Trypanosoma rhodesiense
Vibrio
Yersinia
(treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Corticosteroids, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Nucleoside analogs
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Immunosuppressants
Mycosis
Protozoa
Wound
(treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Arthritis
Asthma
Autoimmune disease
Cachexia
Cirrhosis

Diabetes mellitus
Diarrhea
Multiple sclerosis
Respiratory distress syndrome
(treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-associated, drug targeting with monoclonal antibody to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Cytotoxic agents
(tyrphostins, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(vaginal; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Infection
(viral, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Disease, animal
(wasting, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, n1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, n3, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-2a, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-2b, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lactams
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β1, a, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(γ, 1b, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 37221-79-7, Vasoactive intestinal peptide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonist, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9002-06-6, Thymidine kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 505-60-2, Mustard
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 7585-39-9, β-Cyclodextrin 7585-39-9D, β-Cyclodextrin, hydroxypropyl derivs. 10016-20-3, α-Cyclodextrin 12619-70-4, Cyclodextrin 17465-86-0, γ-Cyclodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as pharmaceutical carrier; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 80-62-6, Methyl methacrylate 2867-47-2, (2-Dimethylaminoethyl) methacrylate 9004-38-0, Cellulose acetate phthalate 34346-01-5, Poly(lactic acid-glycolic acid) 441015-98-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 121749-39-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 54-47-7D, Pyridoxal phosphate, reaction products with Hb conjugates 76-49-3, Bornyl acetate 80-57-9, Verbenone 87-44-5, β-Caryophyllene 88-84-6, β-Guaiene 99-49-0, Carvone 99-83-2, α-Phellandrene 99-87-6, p-Cymene 112-14-1, Octyl acetate 123-35-3, Myrcene 473-11-0, Eudesmane 489-80-5, Guaiane 495-61-4, β-Bisabolene 502-61-4, Farnesene 507-70-0, Borneol 511-59-1, β-Santalene 512-61-8, α-Santalene 515-12-8, Elemane 523-47-7, β-Cadinene 555-10-2, β-Phellandrene 562-74-3, Terpinen-4-ol 1335-14-4 1674-08-4, trans-Pinocarveol 1820-09-3, trans-Ver-benol 2867-05-2, α-Thujene 3856-25-5, α-Copaene 4602-84-0, Farnesol 5208-59-3, β-Bourbonene 6753-98-6, Humulene 6895-56-3, β-Bergamotene 7663-66-3, Bergamotane 8007-35-0, Terpinyl acetate 8013-00-1, Terpinene 10178-38-8, Echinodol 14998-63-1D, Rhenium-186, etidronate complexes, biological studies 17627-44-0, α-Bisabolene 18794-84-8, β-Farnesene 19912-61-9, Furanodiene 20479-06-5, β-Ylangene 21698-66-8, Incensole oxide 21698-67-9, Incensole oxide acetate 22419-74-5, Incensole 25269-16-3, Isocembrene 25322-68-3D, conjugates with pyridoxylated Hb 28028-64-0, Germacrene 29063-28-3, Octanol 29350-73-0, Cadinene 31570-39-5, Cembrene-A 34701-53-6 35731-88-5, Isoincensole oxide 67921-02-2, Cembrenol 94325-73-2 94325-73-2D, compds. 122537-31-9, Oplopane 441771-56-8, Isoincensole 441771-57-9, Isoincensole acetate 441771-74-0, SKB 4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 141436-78-4, Protein kinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 52660-18-1, Casein kinase 1 366806-33-9, Casein kinase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors (ICOS), pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 144114-21-6, HIV-1 Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 70-18-8, Glutathione, biological studies 9030-21-1, Purine nucleoside phosphorylase 9040-48-6, Gelatinase 79747-53-8, Protein tyrosine phosphatase 79955-99-0, Stromelysin 80449-02-1, Tyrosine kinase 106096-93-9, Basic fibroblast growth factor 120178-12-3, Telomerase 131384-38-8, Ras farnesyltransferase 140879-24-9, Proteasome 141256-52-2, Matrilysin 141907-41-7, Matrix metalloproteinase 375798-61-1, Phosphatase, phosphoprotein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9002-61-3, Chorionic gonadotrophin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal antibody to human, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9068-38-6, Reverse transcriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nonnucleoside inhibitors of, pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 1406-18-4, Vitamin E
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oil, as pharmaceutical carrier; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 54-05-7, Chloroquine 54-42-2, Idoxuridine 60-54-8, Tetracycline 69-74-9, Cytarabine Hydrochloride 70-00-8, Trifluridine 80-08-0, Dapsone 90-34-6, Primaquine 100-33-4, Pentamidine 130-95-0, Quinine 443-48-1, Metronidazole 494-79-1, Melarsoprol 665-66-7, Amantadine Hydrochloride 1501-84-4, Rimantadine Hydrochloride 1910-68-5, Methisazone 3056-17-5, d4T 3736-81-0, Diloxanide furoate 5536-17-4, Vidarabine 7481-89-2, DdC 8064-90-2 9004-70-0, HE-2000 10500-82-0, Famotine Hydrochloride 10540-97-3, Memotine Hydrochloride 11006-77-2, Statolon 15176-29-1, Edoxudine 15185-43-0, DOTC 19387-91-8, Tinidazole 19885-51-9, Aranotin 22994-85-0, Benznidazole 23256-30-6, Nifurtimox 25526-93-6, Alovudine 27591-69-1, Tilorone Hydrochloride 27762-78-3, Kethoxal 29984-33-6, Vidarabine Phosphate 30516-87-1, AZT 35607-20-6, Avridine 36791-04-5, Ribavirin 36983-81-0, Fosfonet Sodium 37338-39-9 39809-25-1, Penciclovir 51867-87-9 53230-10-7, Mefloquine 56219-57-9, Arildone 59277-89-3, Acyclovir 63198-97-0, Viroxime

63585-09-1, Foscarnet Sodium 63968-64-9D, Artemisinin, derivs.
68693-30-1, Somantadine Hydrochloride 69123-90-6, Fiacitabine
69123-98-4, Fialuridine 69655-05-6, DdI 69657-51-8, Acyclovir Sodium
69756-53-2, Halofantrine 72301-78-1, Zinviroxime 72301-79-2,
Enviroxime 73514-87-1, Fosarilate 77181-69-2, Sorivudine 80883-55-2,
Enviradene 82410-32-0, Ganciclovir 84408-37-7, Desciclovir
85087-20-3, Doxycycline 87495-31-6, Disoxaril 95233-18-4, Atovaquone
100817-46-7, Stibogluconic acid 104227-87-4, Famciclovir 106362-32-7,
Peptide T 106941-25-7, PMEA 107910-75-8, Ganciclovir Sodium
110042-95-0, Acemannan 110143-10-7, Lodenosine 113852-37-2, Cidofovir
124436-59-5, Pirodavir 124832-27-5, Valacyclovir Hydrochloride
127759-89-1, Lobucavir 127779-20-8, Saquinavir 129618-40-2, Nevirapine
132210-43-6, Cipamfylline 134678-17-4, 3TC 136470-78-5, Abacavir
136817-59-9, Delavirdine 137487-62-8, Alvircept Sudotox 138540-32-6,
Atevirdine Mesylate 141204-94-6, Co-artemether 142340-99-6
142632-32-4, Calanolide A 143491-57-0, Coviracil 145514-04-1, DAPD
147127-20-6, Tenofovir 147221-93-0, Delavirdine Mesylate 147318-81-8,
KNI-272 147362-57-0, Loviride 149845-06-7, Saquinavir Mesylate
149950-60-7, Emivirine 150378-17-9, Indinavir 153127-49-2, ALX40-4C
154598-52-4, DMP 266 155148-31-5, AMD 3100 155213-67-5, Ritonavir
156879-70-8 159519-65-0, Pentafuside 159989-64-7, Nelfinavir
163451-80-7 170020-61-8, FP-21399 174484-41-4, Tipranavir
177932-89-7, DMP-450 178979-85-6, AG 1549 185220-03-5, PNU142721
192725-17-0, ABT-378 214287-88-4, DPC961 216863-66-0, L-756423
251562-00-2, T-1249 383198-56-9, BW 141 383198-57-0, BMS-232630
383198-58-1, PRO 542
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(pharmaceutical formulation further containing; incensole and
furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 50-07-7, Mutamycin 50-18-0, Cyclophosphamide 50-28-2, Estradiol,
biological studies 50-35-1, Thalidomide 50-76-0, Dactinomycin
50-91-9, Floxuridine 51-21-8, Fluorouracil 51-75-2, Mechlorethamine
52-24-4, Thiotepa 53-19-0, Mitotane 53-43-0, DHEA 53-79-2, Puromycin
54-71-7, Pilocarpine hydrochloride 54-91-1, Pipobroman 55-21-0D,
Benzamide, N-substituted compds. 55-86-7, Mechlorethamine Hydrochloride
55-86-7D, Nitrogen mustard, derivs. 55-98-1, Busulfan 56-53-1,
Diethylstilbestrol 57-22-7, Vincristine 57-63-6, Ethinyl oestradiol
57-83-0, Progesterone, biological studies 58-05-9, Leucovorin 58-58-2,
Puromycin Hydrochloride 59-05-2, Methotrexate 66-75-1, Uracil Mustard
83-89-6, Acriquine 101-60-0, Porphyrin 106-60-5, Aminolevulinic acid
114-70-5, Sodium phenylacetate 122-79-2, Phenylacetate 125-45-1,
Azetepa 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 143-67-9,
Vinblastine Sulfate 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3,
Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 302-49-8,
Uredepa 302-79-4, Tretinoin 305-03-3, Chlorambucil 320-67-2,
Azacitidine 359-83-1, Pentazocine 364-62-5, Metoclopramide 366-70-1,
Procarbazine Hydrochloride 378-44-9, Betamethasone 423-55-2,
Perflubron 459-86-9, Mitoguazone 465-65-6, Naloxone 472-15-1,
Betulinic acid 481-29-8, Epiandrosterone 518-28-5, Podophyllotoxin
520-85-4, Medroxyprogesterone 521-12-0, Dromostanolone Propionate
536-59-4, Perillyl alcohol 548-04-9, Hypericin 566-48-3, Formestane
569-57-3, Chlorotrianisene 578-95-0D, Acridone, imidazo derivs.
578-95-0D, Acridone, propylbis derivs. 595-33-5, Megestrol Acetate
645-05-6, Altretamine 646-08-2, β-Alethine 671-16-9, Procarbazine
801-52-5, Porfiromycin 865-21-4, Vinblastine 911-45-5, Clomifene
968-93-4, Testolactone 1271-19-8, Titanocene dichloride 1402-81-9,
Ambomycin 1403-99-2, Mitogillin 1404-00-8, Mitomycin 1404-15-5,
Nogalamycin 1404-20-2, Peliomycin 1404-64-4, Sparsomycin 1661-29-6,

Meturedepa 1972-08-3, Dronabinol 1980-45-6, Benzodepa 2068-78-2, Vincristine Sulfate 2353-33-5, Decitabine 2508-89-6 2608-24-4, Piposulfan 2809-21-4D, Etidronic acid, rhenium-186 complexes 2919-66-6, Melengestrol acetate 2998-57-4, Estramustine 2998-57-4D, Estramustine, analogs 3073-59-4, Hexamethylene bisacetamide 3094-09-5, Doxifluridine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 3930-19-6, Streptonigrin 4105-38-8 4291-63-8, Cladribine 4342-03-4, Dacarbazine 4342-07-8 4803-27-4, Anthramycin 5072-26-4, Buthionine sulfoximine 5373-42-2, Thaliblastine 5508-58-7, Andrographolide 5579-27-1, Simtrazene 5581-52-2, Thiamiprine 5696-17-3, Epipropidine 6157-87-5, Trestolone Acetate 7281-31-4, Vinglycinate Sulfate 7440-06-4D, Platinum, lipophilic compds. or complexes 7440-06-4D, Platinum, triamine complexes 7644-67-9, Azotomycin 7689-03-4D, Camptothecin, derivs. 7724-76-7, Riboprine 7761-45-7, Metoprine 8052-16-2, Cactinomycin 9002-71-5, Thyroid-stimulating hormone 9014-02-2, Zinostatin 9014-42-0, Thrombopoietin 9014-42-0D, Thrombopoietin, mimetics 9015-68-3, Asparaginase 9027-98-9 9041-93-4, Bleomycin Sulfate 9050-67-3, Sizofiran 10043-49-9, Gold-198, biological studies 10087-89-5, Enpromate 10318-26-0, Mitolactol 10403-51-7, Mitindomide 10540-29-1, Tamoxifen 11002-22-5, Apurinic acid 11029-06-4, Elemene 11043-98-4, Mitocromin 11043-99-5, Mitomalcin 11056-06-7, Bleomycin 11056-12-5, Cirolemycin 11056-14-7, Mitocarcin 11056-15-8, Mitosper 12713-07-4D, Verdin, compds. 13010-47-4, Lomustine 13311-84-7, Flutamide 13494-90-1, Gallium nitrate 13665-88-8, Mopidamol 13909-09-6, Semustine 14769-73-4, Levamisole 15475-56-6, Methotrexate Sodium 15639-50-6, Safingol 15663-27-1, Cisplatin 17021-26-0, Calusterone 17902-23-7, Tegafur 18378-89-7, Plicamycin 18416-85-8, Lombricine 18556-44-0, Vinrosidine Sulfate 18588-57-3, Etoprine 18883-66-4, Streptozocin 19916-73-5, O6-Benzylguanine 20098-14-0, Idramantone 20537-88-6, Amifostine 20638-84-0, Retinamide 20830-81-3, Daunorubicin 21059-48-3, Veramine 21679-14-1, Fludarabine 22668-01-5, Etanidazole 23214-92-8, Doxorubicin 23541-50-6, Daunorubicin Hydrochloride 23593-75-1, Clotrimazole 24280-93-1, Mycophenolic Acid 24584-09-6, Dexrazoxane 25316-40-9, Adriamycin 27302-90-5, Oxisuran 27314-97-2, Tirapazamine 27548-93-2D, Baccatin III, derivs. 27686-84-6, Masoprocol 29069-24-7, Prednimustine 29767-20-2, Teniposide 30303-65-2, Docosanol 30387-51-0, Asperlin 30868-30-5, Pyrazofurin 31430-18-9, Nocodazole 31441-78-8, Mercaptopurine 32954-58-8, Ipomeanol 33069-62-4, Paclitaxel 33069-62-4D, Paclitaxel, analogs and derivs. 33419-42-0, Etoposide 35301-24-7, Cedefingol 35846-53-8, Maytansine 35943-35-2, Triciribine 36508-71-1, Zorubicin Hydrochloride 37717-21-8, Flurocitabine 38270-90-5, Strontium Chloride Sr 89 38321-02-7, Dexverapamil 39325-01-4, Picibanil 40391-99-9, Pamidronic acid 41575-94-4, Carboplatin 41729-52-6, Dezaguanine 41992-22-7, Spirogermanium Hydrochloride 42228-92-2, Acivicin 42616-25-1, Methioninase 50264-69-2, Lonidamine 51264-14-3, Amsacrine 51321-79-0, Sparfosic acid 52128-35-5, Trimetrexate 52205-73-9, Estramustine Phosphate Sodium 52794-97-5, Carubicin Hydrochloride 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 54081-68-4, Vinleurosine Sulfate 54824-17-8, Mitonafide 55435-65-9, Acodazole Hydrochloride 56390-09-1, Epirubicin Hydrochloride 56420-45-2, Epirubicin 56605-16-4, Spiromustine 56741-95-8, Bropirimine 57381-26-7, Irsogladine 57576-44-0, Aclarubicin 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57852-57-0, Idamycin 57998-68-2, Diaziquone 58066-85-6, Miltefosine 58525-82-9, Azatyrosine 58957-92-9, Idarubicin 58970-76-6, Ubenimex 59653-73-5, Teroxirone 59917-39-4, Vindesine Sulfate 59989-18-3, 5-Ethynyluracil 60084-10-8, Tiazofurin 60203-57-8, Prostaglandin J2 60940-34-3, Ebselen

61825-94-3, Oxaliplatin 61966-08-3, Triciribine Phosphate 62304-98-7, Thymalfasin 62435-42-1, Perfosfamide 62488-57-7 62816-98-2, Ormaplatin 62928-11-4, Iproplatin 63590-19-2, Balanol 63612-50-0, Nilutamide 63950-06-1, Esorubicin Hydrochloride 65057-90-1, Talisomycin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 65093-40-5, Cytarabine ocfosfate 65222-35-7, Pazelliptine 65271-80-9, Mitoxantrone 65646-68-6, Fenretinide 65807-02-5, Goserelin 65886-71-7, Fazarabine 66569-27-5, Sparfosate Sodium 66849-34-1, Dexifosfamide 67699-41-6, Vinzolidine Sulfate 68278-23-9, Eflornithine Hydrochloride 68475-42-3, Anagrelide 69839-83-4, Didox 70052-12-9, Eflornithine 70384-29-1, Peplomycin Sulfate 70476-82-3, Mitoxantrone Hydrochloride 70641-51-9, Edelfosine 70711-40-9, Ametantrone Acetate 71294-60-5, Rohitukine 71439-68-4, Bisantrene Hydrochloride 71486-22-1, Vinorelbine 71522-58-2, Forfenimex 71628-96-1, Menogaril 72238-02-9D, Retelliptine, demethyl derivs. 72496-41-4, Pirarubicin 72629-69-7, Sarcophytol A 72732-56-0, Piritrexim 72741-87-8, Swainsonine 73105-03-0, Pentamustine 74149-70-5, Parabactin 74381-53-6, Leuprolide Acetate 74790-08-2, Spiroplatin 75219-46-4, Atrimustine 75330-75-5, Lovastatin 75607-67-9, Fludarabine Phosphate 75775-33-6D, Purpurin, compds. 75957-60-7, Splenopentin 76932-56-4, Nafarelin 77016-85-4, Plomestane 77327-05-0, Didemnin B 77599-17-8, Panomifene 77858-21-0, Velaresol 78113-36-7, Romurtide 78186-34-2, Bisantrene 79778-41-9, Neridronic acid 79831-76-8, Castanospermine 80451-05-4, Cecropin B 80576-83-6, Edatrexate 80663-95-2 80841-47-0, Asulacrine 81424-67-1, Caracemide 81965-43-7, SarCNU 82230-03-3, Carbetimer 82413-20-5, Droloxifene 82707-54-8, Neutral endopeptidase 82855-09-2D, Combretastatin, analogs 82952-64-5, Trimetrexate Glucuronate 83086-73-1, Tubulozole Hydrochloride 83150-76-9, Octreotide 83200-11-7, Vinepidine Sulfate 83519-04-4, Ilmofosine 83997-75-5, Iododoxorubicin 84030-84-2, Telluropyrylium 84088-42-6, Roquinimex 84371-65-3, Mifepristone 84412-94-2, Ruboxyl 85465-82-3, Thymotrinan 85622-93-1, Temozolomide 85754-59-2, Ambamustine 85969-07-9, Budotitane 85977-49-7, Tauromustine 86976-56-9, Betaclamycins 87005-03-6, Panaxytriol 87434-82-0, Dezaguanine Mesylate 87806-31-3, Porfimer Sodium 87810-56-8, Fostriecin 87860-39-7, Fostriecin Sodium 88303-60-0, Losoxantrone 88303-61-1, Losoxantrone Hydrochloride 89565-68-4, Tropisetron 89778-26-7, Toremifene 89778-27-8, Toremifene Citrate 90357-06-5, Bicalutamide 90996-54-6, Rhizoxin 92047-76-2, Tetrachlorodecaoxide 92118-27-9, Fotemustine 92788-10-8, Rogletimide 92803-82-2, Aphidicolin glycinate 94079-80-8, Cicaprost 95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 95933-72-5, Amidox 96201-88-6, Brequinar Sodium 96301-34-7, Atamestane 96346-61-1, Onapristone 96389-68-3, Crisnatol 96389-69-4, Crisnatol Mesylate 96392-96-0, Dexormaplatin 96892-57-8, Hepsulfam 97068-30-9, Elsamitrucin 97534-21-9, Merbarone 97682-44-5, Irinotecan 97752-20-0, Droloxifene Citrate 97919-22-7 98319-26-7, Finasteride 98383-18-7, Ecomustine 98631-95-9, Sobuzoxane 99009-20-8, Pyrazoloacridine 99011-02-6, Imiquimod 99283-10-0, Molgramostim 99614-02-5, Ondansetron 100286-90-6, Irinotecan Hydrochloride 100324-81-0, Lisofylline 102396-24-7, Jasplakinolide 102676-31-3, Fadrozole Hydrochloride 102676-47-1, Fadrozole 102822-56-0, Mannostatin A 103222-11-3, Vapreotide 103612-80-2 104493-13-2, Adecypenol 105118-12-5, Piroxantrone Hydrochloride 105149-04-0, Osaterone 105615-58-5, Oxaunomycin 105844-41-5, Plasminogen activator inhibitor 106096-93-9D, Basic Fibroblast growth factor, saporin

conjugates 106400-81-1, Lometrexol 107000-34-0, Zanoterone 107256-99-5, Tamoxifen methiodide 107868-30-4, Exemestane 108736-35-2, Lanreotide 108852-90-0, Nemorubicin 109837-67-4, Cycloplatam 110267-81-7, Amrubicin 110311-27-8, Sulofenur 110314-48-2, Adozelesin 110690-43-2, Emitefur 110942-02-4, Aldesleukin 110942-08-0, Luprolide 111490-36-9, Zeniplatin 111523-41-2, Enloplatin 112515-43-2, Topsentin 112522-64-2, Acetyldinaline 112809-51-5, Letrozole 112859-71-9, Fluasterone 112887-68-0, Raltitrexed 112965-21-6, Calcipotriol 114084-78-5, Ibandronic acid 114285-68-6, Lentinan sulfate 114517-02-1, Fosquidone 114977-28-5, Taxotere 115150-59-9, Antagonist G 115308-98-0, Tallimustine 115566-02-4, Bistratene A 115575-11-6, Liarozole 115956-12-2, Dolasetron 116057-75-1, Idoxifene 117048-59-6, Combretastatin A4 117091-64-2, Etoposide Phosphate 118292-40-3, Tazarotene 119169-78-7, Epristeride 119413-54-6, Topotecan Hydrochloride 119813-10-4, Carzelesin 120287-85-6, Cetrorelix 120408-07-3, Lometrexol Sodium 120500-15-4, Leinamycin 120511-73-1, Anastrozole 120685-11-2, Benzoylstaurosporine 121181-53-1, Filgrastim 121263-19-2, Calphostin C 121288-39-9, Loxoribine 121547-04-4, Mirimostim 122111-03-9, Gemcitabine Hydrochloride 122341-38-2, Temoporfin 122431-96-3 122898-63-9, Phenazinomycin 123040-69-7, Azasetron 123258-84-4, Itasetron 123760-07-6, Zinostatin stimalamer 123774-72-1, Sargramostim 123830-79-5, Teloxantrone Hydrochloride 123948-87-8, Topotecan 124012-42-6, Galocitabine 124689-65-2D, Cryptophycin A, derivs. 124784-31-2, Erbulozole 124904-93-4, Ganirelix 125317-39-7, Vinorelbine Tartrate 125392-76-9, Acylfulvene 125533-88-2, Mofarotene 126297-39-0, Lissoclinamide 7 126443-96-7, Napavin 127984-74-1, Lanreotide Acetate 128505-88-4, Naphterpin 128768-09-2, Placetin A 128768-11-6, Placetin B 129497-78-5, Verteporfin 129564-92-7, Azatoxin 129655-21-6, Bizelesin 129731-10-8, Vorozole 130167-69-0, Pegaspargase 130288-24-3, Duocarmycin SA 130364-39-5, Rubiginone B1 130370-60-4, Batimastat 131190-63-1, Saintopin 132036-88-5, Ramosetron 132073-72-4, Tetrazomine 133432-71-0, Peldesine 134088-74-7, Nartograstim 134381-30-9, Conagenin 134523-84-5 134633-29-7, Tecogalan Sodium 134861-62-4, Dioxamycin 135257-45-3, Crambescidin 816 135381-77-0, Flezelastine 135383-02-7, Stipiamide 135558-11-1, Lobaplatin 135819-69-1 135968-09-1, Lenograstim 137018-54-3, Okicenone 137099-09-3, Turosteride 137219-37-5, Dehydrodidemnin B 137647-92-8, Axinastatin 1 137964-32-0 139755-79-6, Safingol Hydrochloride 140207-93-8, Pentosan polysulfate sodium 140703-49-7, Meterelin **142880-36-2**, Ilomastat 144885-51-8, Sodium borocaptate 144916-42-7, Sonermin 145124-30-7, Bisnafide dimesylate 145858-50-0, Liarozole Hydrochloride 146426-40-6, Flavopiridol 148317-76-4, Oracin 148584-53-6 148717-58-2, Palauamine 148717-90-2, Squalamine 149204-42-2, Kahalalide F 149260-80-0, Mycaperoxide B 149355-77-1, Lamellarin-N triacetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 149633-91-0, Leptolstatin 149715-96-8, Spongistatin 1 149882-10-0, Lurtotecan 150829-93-9, Nisamycin 151272-78-5, Antarelix 152923-56-3, Dacliximab 153723-34-3, Axinastatin 2 153723-35-4, Axinastatin 3 154039-60-8, Marimastat 154229-19-3, Abiraterone 154248-96-1, Iroplact 154277-21-1, Cypemycin 154361-50-9, Capecitabine 155233-30-0, Curacin A 156586-89-9, Edrecolomab 156790-85-1, Variolin B 156856-30-3, Cytostatin 157078-48-3, Isohomohalichondrin B 157857-21-1, Maspin 158792-24-6, Collismycin A 158792-25-7, Collismycin B 168482-36-8, Cryptophycin 8 172793-30-5 173046-02-1,

Thiocoraline 174305-65-8, Breflate 181887-82-1, Nitrullin 188364-40-1, CARN 700 200139-38-4, Suradista 212894-59-2, Pentrozole 246252-04-0, Lutetium texaphyrin 246252-06-2, Gadolinium texaphyrin 284041-10-7 324740-00-3, Vitaxin 441070-87-7, 1,2,3-Triazolecarboxamide 441070-88-8 441070-92-4 441772-39-0, Isobengazole 441772-43-6, Nagrestip 441772-66-3, Vinxaltine 441772-81-2, Sulfmosine 441774-07-8, Spicamycin D 441774-77-2, Solverol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 60529-76-2, Thymopoietin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor agonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 79217-60-0, Cyclosporin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 50-07-7, Mitomycin C 1397-89-3, Amphotericin B
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

L59 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:332055 HCAPLUS
DN 136:350543
ED Entered STN: 03 May 2002
TI Metalloprotease inhibitors for treatment of **angiogenesis**
IN Pan, Duojia; Rubin, Gerald M.; Zhang, Hongbing
PA The Regents of the University of California, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K039-00
ICS A61K039-395; A61K049-00; C12Q001-00; G01N033-53; G01N033-48
CC 1-6 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002034289	A1	20020502	WO 2001-US45612	20011025
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6436629	B1	20020820	US 2000-697854	20001027
AU 2002020098	A5	20020506	AU 2002-20098	20011025
EP 1333856	A1	20030813	EP 2001-988593	20011025

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2002132778 A1 20020919 US 2002-68591 20020206

PRAI US 2000-697854 A 20001027

WO 2001-US45612 W 20011025

AB The invention provides methods and compns. relating to Kuz involvement in angiogenesis. In various embodiments, the invention provides methods for modulating angiogenesis by specifically modulating the activity of Kuz in a vertebrate animal predetd. to have a pathogenic angiogenesis; and subsequently detecting a resultant angiogenic modulation in the animal. Methods are provided for identifying a modulator of angiogenesis by (a) contacting an angiogenic assay system comprising a predetd. amount of Kuz with a candidate agent, under conditions whereby but for the presence of the agent, the system provides a reference angiogenesis; and (b) detecting an agent-biased angiogenesis of the system.

ST **angiogenesis** antitumor metalloprotease inhibitor Kuz protein

IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Kuz mutant fused to Fc region of; metalloprotease inhibitors for treatment of **angiogenesis**)

IT Antibodies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Kuz-specific; metalloprotease inhibitors for treatment of **angiogenesis**)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Kuzbanian (Kuz); metalloprotease inhibitors for treatment of **angiogenesis**)

IT Carboxylic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carboxylates; metalloprotease inhibitors for treatment of **angiogenesis**)

IT Hydroxamic acids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxamates; metalloprotease inhibitors for treatment of **angiogenesis**)

IT **Angiogenesis inhibitors**
Antitumor agents
Chelating agents
(metalloprotease inhibitors for treatment of **angiogenesis**)

IT Flavanols
Thiols (organic), biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metalloprotease inhibitors for treatment of **angiogenesis**)

IT 81669-70-7, Metalloprotease 151769-16-3, TACE
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; metalloprotease inhibitors for treatment of **angiogenesis**)

IT 60-00-4, EDTA, biological studies 66-71-7, 1,10-Phenanthroline 120-80-9D, o-Hydroxyphenol, derivs. 130370-60-4, Batimastat **142880-36-2**, GM6001 **421553-77-7**, IC 3 421567-09-1, GW 9471
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metalloprotease inhibitors for treatment of **angiogenesis**)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Fambrough; Proc Natl Acad Sci 1996, V93, P13233 HCAPLUS
(2) Pan; Cell 1997, V90, P271 HCAPLUS
(3) Wen; Development 1997, V124, P4759 HCAPLUS

L59 ANSWER 12 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2002045613 EMBASE
TI Up-regulation of vascular endothelial growth factor by membrane-type 1 matrix metalloproteinase stimulates human glioma xenograft growth and angiogenesis.
AU Deryugina E.I.; Soroceanu L.; Strongin A.Y.
CS A.Y. Strongin, Burnham Institute, 10901 North Torrey Pines Road, San Diego, CA 92037, United States. strongin@burnham.org
SO Cancer Research, (15 Jan 2002) 62/2 (580-588).
Refs: 66
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB Membrane-type (MT) 1 matrix metalloproteinase (MMP) is up-regulated in many tumor types and has been implicated in tumor progression and metastasis. MT1-MMP is critical for pericellular degradation of the extracellular matrix, thereby promoting tumor cell invasion and dissemination. To grow efficiently in vivo, tumor cells induce angiogenesis in both primary solid tumors and metastatic foci. The present study describes a functional link between the expression of MTI-MMP and vascular endothelial growth factor (VEGF) production in human glioma U251 xenografts in athymic mice. To investigate the effects of MT1-MMP on VEGF expression, U251 cells were stably transfected with MT1-MMP to generate the U-MT cell line overexpressing the enzyme. In vitro, the U-MT cells had an increased rate of proliferation and migration as well as the ability to activate the MMP-2 proenzyme and directionally remodel a three-dimensional collagen matrix. These findings suggested higher tumorigenicity of U-MT cells relative to the vector-control U-neo cells. In agreement with the in vitro data, U-MT xenografts in BALB/c nu/nu mice displayed markedly increased growth rates and elevated levels of angiogenesis. In contrast, U-neo cells formed small, minimally vascularized tumors. The elevated angiogenesis in U-MT xenografts was associated with an up-regulation of VEGF expression in tumor cells. In addition, U-MT cells in vitro secreted twice as much VEGF as the control cells. GM6001, a hydroxamate inhibitor of MMP activity, down-regulated the production of VEGF in U-MT cells to the levels observed in the U-neo control. Our results demonstrate that the enhanced tumorigenicity of glioma cells overexpressing MT1-MMP involves stimulation of angiogenesis through the up-regulation of VEGF production.
CT Medical Descriptors:
*glioma
*cancer growth
***tumor vascularization**
*angiogenesis
*metastasis: ET, etiology
tumor xenograft

protein induction
extracellular matrix
cancer invasion
in vivo study
protein expression
cancer cell culture
genetic transfection
in vitro study
cell proliferation
cell migration
enzyme activation
carcinogenicity
comparative study
mouse strain
growth rate
cancer inhibition
human
nonhuman
mouse
animal experiment
animal model
controlled study
human cell
animal tissue
article
priority journal
Drug Descriptors:
*vasculotropin: EC, endogenous compound
*matrix metalloproteinase 14: EC, endogenous compound
gelatinase A
enzyme precursor
collagen
ilomastat: PD, pharmacology
hydroxamic acid derivative: PD, pharmacology
RN (vasculotropin) 127464-60-2; (gelatinase A) 146480-35-5; (collagen) 9007-34-5; (ilomastat) **142880-36-2**
CN (1) Gm 6001
CO (1) AMS (United States)

L59 ANSWER 13 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:510092 BIOSIS
DN PREV200200510092
TI Investigation of the invasive capacity of basal cell carcinoma using an invasion assay model.
AU Lim, P. [Reprint author]; Wilson, G. D.; Sanders, R. [Reprint author]
CS RAFT Institute of Plastic Surgery and Gray Cancer Institute, Northwood, Middlesex, UK
SO British Journal of Cancer, (June, 2002) Vol. 86, No. Supplement 1, pp. S81. print.
Meeting Info.: British Cancer Research Meeting 2002. Glasgow, UK. June 30-July 03, 2002.
CODEN: BJCAAI. ISSN: 0007-0920.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 2 Oct 2002
Last Updated on STN: 2 Oct 2002
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Human 02508

Enzymes - General and comparative studies: coenzymes 10802
Pathology - General 12502
Pathology - Therapy 12512
Integumentary system - Physiology and biochemistry 18504
Integumentary system - Pathology 18506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
IT Major Concepts
Integumentary System (Chemical Coordination and Homeostasis); Pharmacology; **Tumor** Biology
IT Diseases
basal cell carcinoma: integumentary system disease, neoplastic disease, pathology
Carcinoma, Basal Cell (MeSH)
IT Chemicals & Biochemicals
TIMP-2 [tissue **inhibitor** of **metalloproteinase**-2]: expression; ilomastat: enzyme inhibitor-drug; matrix metalloproteinase-2 [MMP-2]: expression
IT Methods & Equipment
invasion assay model: evaluation method
IT Miscellaneous Descriptors
tumor invasiveness; Meeting Abstract
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
KMC-1 cell line: human basal cell carcinoma cells
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 124861-55-8 (TIMP-2)
124861-55-8 (tissue **inhibitor** of **metalloproteinase**-2)
142880-36-2 (ilomastat)
146480-35-5 (matrix metalloproteinase-2)
146480-35-5 (MMP-2)

L59 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:15004 HCAPLUS
DN 132:73666
ED Entered STN: 07 Jan 2000
TI Ophthalmic uses of PPAR-γ agonists and antagonists
IN Pershadsingh, Harrihar A.; Levy, Daniel E.
PA Photogenesis, Inc., USA
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-425
CC 1-12 (Pharmacology)
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000000194	A1	20000106	WO 1999-US14262	19990625

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 9947134	A1	20000117	AU 1999-47134	19990625
	US 6316465	B1	20011113	US 1999-342381	19990628
PRAI	US 1998-90937P	P	19980627		
	US 1998-90937	P	19980627		
	WO 1999-US14262	W	19990625		

OS MARPAT 132:73666

AB Methods are disclosed for treating diseases of ocular tissues expressing the nuclear receptor PPAR-γ, by inhibiting the inflammatory response, the neovascularization and angiogenesis, and programmed cell death (apoptosis) in these target tissues, comprising administering to a human or animal in need of treatment an effective amount of a compound that modifies the activity of PPAR-γ, or a pharmaceutically acceptable salt or solvate thereof. Novel compds. and methods for their synthesis are provided.

ST eye disease PPARgamma agonist antagonist; inflammation **neovascularization** eye PPARgamma agonist antagonist; **angiogenesis** apoptosis eye PPARgamma agonist antagonist

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Diterpenes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carboxy; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye
(choroid, choroiditis and idiopathic central serous choroidopathy; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye
(conjunctiva, ulcer; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye, disease
(conjunctivitis; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Antiulcer agents
(corneal or conjunctival ulcer; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye, disease
(diabetic retinopathy; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Toxicity
(drug, retinal toxicosis; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye, disease
(endophthalmitis; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye, disease
(inflammation; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Surgery
(intraocular, retinopathy associated with; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye, disease
(iridocyclitis; ophthalmic uses of PPAR-γ agonists and

antagonists)
IT Eye, disease
(keratitis; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(keratopathy, inflammation, and **neovascular** proliferative disease; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(keratopathy, ulcer; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(macula, degeneration; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(macula, senile degeneration; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Edema
(macular; ophthalmic uses of PPAR-γ agonists and antagonists)
IT **Angiogenesis**
Angiogenesis
(**neovascularization**, eye; ophthalmic uses of PPAR-γ agonists and antagonists)
IT **Angiogenesis**
(**neovascularization**, retinal; ophthalmic uses of PPAR-γ agonists and antagonists)
IT **Eye, disease**
(**neovascularization**; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Blood vessel, disease
(occlusion; ophthalmic uses of PPAR-γ agonists and antagonists)
IT **Angiogenesis inhibitors**
Anti-inflammatory agents
Apoptosis
Cell death
Cytotoxic agents
Eye, disease
Glaucoma (disease)
(ophthalmic uses of PPAR-γ agonists and antagonists)
IT Proliferation inhibition
(proliferation inhibitors; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Drugs
(retinal toxicosis; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(retinitis; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Aneurysm
(retinopathy associated with telangiectasias or; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Myasthenia gravis
(retinopathy associated with uveoretinitis or; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Lupus erythematosus
Multiple sclerosis
Rheumatoid arthritis
(retinopathy associated with; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(retinopathy, degeneration; ophthalmic uses of PPAR-γ agonists and antagonists)

IT Eye, disease
(retinopathy, detachment, primary or secondary, from disease or injury; ophthalmic uses of PPAR-γ agonists and antagonists)
IT **Eye, disease**
(retinopathy, **neovascularization**; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(retinopathy; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Blood vessel, disease
(retinovascular disease; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye
(uvea, inflammation and **neovascular** proliferative disease; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(uveitis, and panuveitis; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye, disease
(uveoretinitis; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Eye
(vitreous humor, vitreitis; ophthalmic uses of PPAR-γ agonists and antagonists)
IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; ophthalmic uses of PPAR-γ agonists and antagonists)
IT 302-79-4, Retinoic acid 506-32-1D, Arachidonic acid, metabolites 2295-31-0D, Thiazolidinedione, derivs. 5067-18-5, Auronol 60203-57-8, Prostaglandin J2 60203-57-8D, Prostaglandin J2, metabolites 74772-77-3, Ciglitazone 82508-31-4, Pseudolaric acid B 87893-55-8 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 141200-24-0, Darglitazone 196814-73-0D, derivs. 253587-89-2 253587-91-6 **253587-93-8** 253587-96-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ophthalmic uses of PPAR-γ agonists and antagonists)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Vyas; US 5700820 A 1997

L59 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:231223 HCAPLUS
DN 130:252675
ED Entered STN: 14 Apr 1999
TI Process for the preparation of N-acyl-L-tryptophan carboxamide derivatives as synthetic matrix metalloprotease inhibitors
IN Levy, Daniel E.; Grobelny, Damian; Tang, Cho; Holme, Kevin R.; Galardy, Richard E.; Schultz, Gregory S.; Nematalia, Asaad; Musser, John H.
PA Glycomed Incorporated, USA; The University of Florida
SO U.S., 46 pp., Cont.-in-part of U.S. Ser. No. 44,324.
CODEN: USXXAM
DT **Patent**
LA English
IC ICM C07B057-00
ICS C07C227-18; C07C235-16; C07D209-20
NCL 564133000
CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 7, 63

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5892112	A	19990406	US 1994-184727	19940121
	US 5114953	A	19920519	US 1990-616021	19901121
	US 5183900	A	19930202	US 1990-615798	19901121
	US 5189178	A	19930223	US 1991-747752	19910820
	US 5239078	A	19930824	US 1991-747751	19910820
	CA 2096225	AA	19930221	CA 1991-2096225	19911121
	US 5268384	A	19931207	US 1992-817039	19920107
	US 5270326	A	19931214	US 1992-881630	19920512
	US 5696147	A	19971209	US 1993-161786	19931203
	US 5773438	A	19980630	US 1994-464927	19940605
	CA 2158760	AA	19950727	CA 1995-2158760	19950120
	WO 9519965	A1	19950727	WO 1995-US783	19950120
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9516049	A1	19950808	AU 1995-16049	19950120
	EP 690841	A1	19960110	EP 1995-908086	19950120
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09501183	T2	19970204	JP 1995-519668	19950120
	AU 9883118	A1	19990128	AU 1998-83118	19980904
	AU 9910003	A1	19990304	AU 1999-10003	19990104
PRAI	US 1990-616021	A1	19901120		
	US 1990-615798	A2	19901121		
	US 1991-747751	A1	19910820		
	US 1991-747752	A2	19910820		
	US 1992-817039	A2	19920107		
	US 1992-881630	A1	19920512		
	US 1993-44324	A2	19930407		
	US 1990-477751	B2	19900209		
	US 1991-615798	A	19911121		
	US 1994-184727	A3	19940121		
	AU 1994-65542	A3	19940401		
	AU 1995-16049	A3	19950120		
	WO 1995-US783	W	19950120		
OS	MARPAT 130:252675				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for the preparation of N-acyl-L-tryptophan derivs. I [R1 = H, alkyl; R2 = H, alkyl, NHZ; Z = R11, COR11, CO2R11; R11 = alkyl; R1R2 = (CH2)p; p = 3-5; R3 = H, C1-4 alkyl; R4 = Me, fused or conjugated, (un)substituted bicycloarylmethylene; n = 0-2; X = OR5, NHR5, NR5R5, NH(CH2)q, M; R5 = independently H, (un)substituted alkyl, (un)substituted aryl, (un)substituted arylalkyl; q = 1-8; M = amino acid residue, amino acid amide residue, cyclic amino, heterocyclic amino; R6 = H, lower alkyl; R7 = H, lower alkyl, acyl] as synthetic mammalian matrix metalloprotease inhibitors are disclosed that are useful for treating or preventing diseases wherein said diseases are caused by unwanted mammalian matrix metalloprotease activity and include skin disorders, keratoconus, restenosis, rheumatoid arthritis, wounds, cancer, angiogenesis and shock. Thus, benzyl 4-methyl-2-oxopentanoate underwent Wittig reaction with Ph3P:CHCO2Me (100%), hydrogenation of the formed unsatd. diester (86%),

peptide coupling of the obtained monoacid with H-Trp-NHMe.HCl and separation of diastereomers (83%), and reaction with NH2OH (56% and 72%), to give isomeric title compds. II and III. II inhibited 72 kD gelatinase with Ki = 0.26 nM and 92 kD gelatinase with Ki = 0.22 nM. Procedures using II for the inhibition of angiogenesis, treatment of psoriasis, treatment of chronic dermal wounds, treatment of thioglycollate-induced peritonitis, antimetastasis activity, treatment of hypovolumic shock, and antirestenotic activity are also given.

ST acyltryptophan amide prepn process matrix metalloproteinase inhibitor; **angiogenesis** inhibitor acyltryptophan amide prepn process; chronic dermal wound treatment acyltryptophan amide prepn process; peritonitis treatment acyltryptophan amide prepn process; hypovolumic shock treatment acyltryptophan amide prepn process; metastasis inhibitor acyltryptophan amide prepn process; restenosis inhibitor acyltryptophan amide prepn process

IT Artery, disease
(coronary, restenosis; process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT Antitumor agents
(metastasis; process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT Peritoneum
(peritonitis; process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT **Angiogenesis inhibitors**
Psoriasis
Shock (circulatory collapse)
Wound healing promoters
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT 146480-35-5, 72,000-Mol.-weight gelatinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(natural human; process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT **142880-36-2P 142880-37-3P 142880-75-9P**
171347-76-5P 171347-96-9P 221622-85-1P 221622-91-9P 221622-92-0P
221623-01-4P 221623-07-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT **142880-38-4P 142880-62-4P** 142880-66-8P 142880-72-6P
142880-73-7P 144070-01-9P **162550-05-2P** 171347-75-4P
171347-77-6P **171347-80-1P 171347-81-2P**
171347-82-3P 171347-83-4P 171347-85-6P
200959-08-6P 221622-65-7P 221622-67-9P
221622-69-1P 221622-71-5P 221622-73-7P
221622-75-9P 221622-77-1P 221622-78-2P 221622-79-3P
221622-81-7P **221622-82-8P 221622-83-9P**
221622-86-2P 221622-88-4P 221622-89-5P 221622-90-8P
221622-94-2P 221622-95-3P **221622-97-5P** 221623-03-6P
221623-08-1P 221623-11-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as

synthetic matrix metalloprotease inhibitors)

IT 79955-99-0, Stromelysin 146480-36-6, 92,000-Mol.-weight gelatinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT 141907-41-7, Matrix metalloproteinase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT 64-04-0, 2-Phenylethylamine 65-85-0, Benzoic acid, reactions 73-22-3, L-Tryptophan, reactions 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 108-31-6, 2,5-Furandione, reactions 108-91-8, Cyclohexylamine, reactions 109-55-7 115-11-7, 2-Methylpropene, reactions 123-00-2, 4-Morpholinepropanamine 124-09-4, 1,6-Hexanediamine, reactions 459-46-1, p-Fluorobenzyl bromide 2038-03-1, 4-Morpholineethanamine 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 2627-86-3, (S)-α-Methylbenzylamine 3731-53-1, 4-Aminomethylpyridine 4502-00-5, Sodium 4-methyl-2-oxopentanoate 5437-45-6, Bromoacetic acid benzyl ester 13139-14-5 13149-00-3, cis-1,2-Cyclohexanedicarboxylic anhydride 14166-21-3, trans-1,2-Cyclohexanedicarboxylic anhydride 35303-76-5, 4-(2-Aminoethyl)benzenesulfonamide 35793-73-8 35858-81-2, L-Tryptophan benzyl ester hydrochloride 51186-58-4 53064-79-2, Iodomethyl pivalate 53708-63-7 69621-45-0 111372-25-9, L-Tryptophan dodecylamide 112245-04-2 119893-56-0 142880-44-2 142880-45-3 142880-47-5 142880-55-5, L-Tryptophan piperidinamide 142902-74-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT 1676-74-0P, L-Tryptophan N-carboxyanhydride 14035-83-7P, Isobutylsuccinic anhydride 18908-20-8P, β-Methallylsuccinic anhydride 66095-18-9P 96136-13-9P, Benzyl 4-methyl-2-oxopentanoate 111955-05-6P 132631-36-8P, 2-Isobutyl-3-(methoxycarbonyl)propionic acid 142880-33-9P 142880-34-0P 142880-35-1P 142880-63-5P 142880-64-6P 142880-65-7P 142902-75-8P 144070-02-0P 144070-04-2P 149821-14-7P 152993-11-8P 162550-03-0P 162678-79-7P 171347-89-0P 171347-90-3P 171347-94-7P 171347-95-8P **171347-98-1P** 171347-99-2P **171348-01-9P 171348-03-1P 171348-04-2P** 171348-08-6P 171348-09-7P 171483-46-8P 186969-64-2P 221622-63-5P 221622-64-6P 221622-66-8P 221622-68-0P 221622-70-4P 221622-72-6P 221622-74-8P 221622-76-0P 221622-84-0P 221622-87-3P 221622-93-1P **221622-96-4P** 221622-99-7P 221623-05-8P 221623-09-2P 221623-10-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

IT 9001-12-1, Collagenase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(recombinant neutrophil and human gingivival fibroblast; process for preparation of N-acyl-L-tryptophan carboxamide derivs. as synthetic matrix metalloprotease inhibitors)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; EP 0236872 B1 1987 HCAPLUS
(2) Anon; EP 0236872 1987 HCAPLUS

(3) Anon; EP 0445206 B1 1989 HCAPLUS
(4) Anon; EP 446257 A 1991
(5) Anon; EP 0574758 A1 1993 HCAPLUS
(6) Anon; EP 0575844 A2 1993 HCAPLUS
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(8) Dean; J Chem Soc 1965, P6655 HCAPLUS
(9) Dickens; US 4599361 1986 HCAPLUS
(10) Dickens; US 4743587 1988 HCAPLUS
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(19) Tanzawa; J Antibiot 1992, V45(11), P1733 HCAPLUS
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L59 ANSWER 16 OF 25 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:482830 BIOSIS
DN PREV199900482830
TI Functional overlap between two classes of matrix-degrading proteases in wound healing.
AU Lund, Leif R.; Romer, John; Bugge, Thomas H.; Nielsen, Boye S.; Frandsen, Thomas L.; Degen, Jay L.; Stephens, Ross W.; Dano, Keld [Reprint author]
CS The Finsen Laboratory, Rigshospitalet, Strandboulevarden 49, DK-2100, Copenhagen O, Denmark
SO EMBO (European Molecular Biology Organization) Journal, (Sept. 1, 1999) Vol. 18, No. 17, pp. 4645-4656. print.
CODEN: EMJODG. ISSN: 0261-4189.
DT Article
LA English
ED Entered STN: 16 Nov 1999
Last Updated on STN: 5 Jun 2000
AB Retarded wound healing was found in mice deficient in the serine protease precursor plasminogen, as well as in wild-type mice treated with the **metalloprotease inhibitor** galardin, but in both cases wound closure was ultimately completed in all mice within 60 days. The expression of several matrix metalloproteases in keratinocytes migrating to cover the wound was strongly enhanced by galardin treatment. However, when plasminogen-deficient mice were treated with galardin, healing was completely arrested and wound closure was not seen during an observation period of 100 days, demonstrating that protease activity is essential for skin wound healing. The requirement for both plasminogen deficiency and **metalloprotease inhibition** for complete inhibition of the healing process indicates that there is a functional overlap between the two classes of matrix-degrading proteases, probably in the dissection of the fibrin-rich provisional matrix by migrating keratinocytes. Each class alone is capableof maintaining sufficient keratinocyte migration to regenerate the epidermal surface, although this function would normally be performed by both classes acting in parallel. Since there are strong similarities between the proteolytic mechanisms in wound healing and **cancer** invasion, these results predict that complete arrest of this latter process in therapeutic settings will require the use of inhibitors of both classes of proteases.
CC Enzymes - Chemical and physical 10806
Cytology - Animal 02506

Anatomy and Histology - Regeneration and transplantation 11107
Integumentary system - Pathology 18506
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
General biology - Miscellaneous 00532
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Integumentary System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
keratinocytes: integumentary system
IT Chemicals & Biochemicals
galardin: enzyme inhibitor; metalloprotease
IT Miscellaneous Descriptors
skin wound healing
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN **142880-36-2** (galardin)
81669-70-7 (metalloprotease)

L59 ANSWER 17 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2000050153 EMBASE
TI Present status and future strategy for clinical development of antimetastatic drugs.
AU Sone S.
CS Dr. S. Sone, Third Dept. of Internal Medicine, Univ. of Tokushima Sch. of Medicine, 3-18-15 Kuramoto-cho, Tokushima 770-8503, Japan
SO Biotherapy, (1999) 13/12 (1215-1222).
Refs: 11
ISSN: 0914-2223 CODEN: BITPE
CY Japan
DT Journal; General Review
FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
LA Japanese
SL English; Japanese
AB Recently, much attention has been paid to the clinical development of antimetastatic drugs targeting the important molecules involved in cell growth, invasion, metastatic formation of cancer cells and tumor angiogenesis. Among them, several drugs are designed to inhibit those activities, by which cancer metastasis may be controlled. A future strategy is required in order to evaluate the efficacy of these new antimetastatic drugs in combination with conventional anticancer therapy (surgery, radiotherapy and chemotherapy). For this, careful consideration must be taken in the design of phase III trials. This paper reviews the present status of ongoing clinical trials and the future strategy for development of new antimetastatic drugs.
CT Medical Descriptors:
*metastasis inhibition
*cancer: DT, drug therapy
tumor vascularization

cancer growth
cell invasion
drug research
human
clinical trial
controlled study
review
Drug Descriptors:
*angiogenesis inhibitor: CT, clinical trial
*angiogenesis inhibitor: DT, drug therapy
*angiogenesis inhibitor: PD, pharmacology
*antimetastatic agent: CT, clinical trial
*antimetastatic agent: DT, drug therapy
*antimetastatic agent: PD, pharmacology
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT, clinical trial
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT, drug therapy
3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD, pharmacology
suramin: CT, clinical trial
suramin: DT, drug therapy
suramin: PD, pharmacology
leflunomide: CT, clinical trial
leflunomide: DT, drug therapy
leflunomide: PD, pharmacology
alpha interferon: CT, clinical trial
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
squalamine: CT, clinical trial
squalamine: DT, drug therapy
squalamine: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: DT, drug therapy
thalidomide: PD, pharmacology
cm 101: CT, clinical trial
cm 101: DT, drug therapy
cm 101: PD, pharmacology
fumagillol chloroacetylcarbamate: CT, clinical trial
fumagillol chloroacetylcarbamate: DT, drug therapy
fumagillol chloroacetylcarbamate: PD, pharmacology
monoclonal antibody lm 609: CT, clinical trial
monoclonal antibody lm 609: DT, drug therapy
monoclonal antibody lm 609: PD, pharmacology
cgs 27023a: CT, clinical trial
cgs 27023a: DT, drug therapy
cgs 27023a: PD, pharmacology
ag 3340: CT, clinical trial
ag 3340: DT, drug therapy
ag 3340: PD, pharmacology
marimastat: CT, clinical trial
marimastat: DT, drug therapy
marimastat: PD, pharmacology
batimastat: CT, clinical trial
batimastat: DT, drug therapy
batimastat: PD, pharmacology
ilomastat: CT, clinical trial
ilomastat: DT, drug therapy
ilomastat: PD, pharmacology

RN (3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one) 186610-95-7; (suramin) 129-46-4, 145-63-1; (leflunomide) 75706-12-6; (squalamine) 148717-90-2, 160022-48-0; (thalidomide) 50-35-1; (cm 101) 188417-67-6; (fumagillol chloroacetylcarbamate) 129298-91-5; (cgs 27023a) 169799-04-6; (ag 3340) 195008-93-6; (marimastat) 154039-60-8; (batimastat) 130370-60-4, 130464-84-5; (ilomastat) **142880-36-2**

L59 ANSWER 18 OF 25 EMBASE
on STN
AN 1999113123 EMBASE
TI Antiangiogenic agent derived from inhibition of MMP.
AU Arii S.; Imamura M.
CS Dr. S. Arii, Dept. of Surg. and Surg. Basic Sci., Kyoto Univ. Graduate Sch. of Med., 54 Shogoin-Kawara-cho, Sakyo-ku, Kyoto 606-8507, Japan
SO Biotherapy, (1999) 13/2 (154-159).
Refs: 13
ISSN: 0914-2223 CODEN: BITPE
CY Japan
DT Journal; Article
FS 016 Cancer
037 Drug Literature Index
LA Japanese
SL English; Japanese
AB Degradation of the basement membrane and invasion to the extracellular matrix of vascular endothelial cells is considered to be the initial step in angiogenesis. MMP (matrix metalloproteinase) and TIMP (tissue inhibitor of metalloproteinase) are deeply involved in the angiogenic cascade. In this article, we describe antiangiogenic agents which function by inhibiting MMP, particularly Batimastat (BB94) and PEX. Batimastat is a low molecular synthetic inhibitor which works on a wide range against various MMP. This agent demonstrates angiostatic activity in vivo and inhibition of both tumor growth and metastasis. PEX is a hemopexin-like domain located on the C- terminal of MMP-2, which inhibits the binding of MMP2, and α v β3 integrin, thereby suppressing MMP-2 function and inhibiting angiogenesis and tumor growth. Thus, owing to their antiangiogenic potential and inhibitory action against extracellular matrix degradation, MMP inhibitors seem to be unique and promising therapeutic agents against cancer.
CT Medical Descriptors:
*angiogenesis
extracellular matrix
vascular endothelium
cancer inhibition
tumor vascularization
tumor growth
antineoplastic activity
drug mechanism
article
Drug Descriptors:
*angiogenesis inhibitor: PD, pharmacology
*matrix metalloproteinase: EC, endogenous compound
*batimastat: PD, pharmacology
*gelatinase a: EC, endogenous compound
ilomastat
tissue inhibitor of metalloproteinase: EC, endogenous compound
RN (batimastat) 130370-60-4, 130464-84-5; (gelatinase a) 146480-35-5; (ilomastat) **142880-36-2**; (tissue inhibitor of metalloproteinase) 97837-28-0
CN Bb 94; Gm 6001

L59 ANSWER 19 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999298824 EMBASE
TI Theoretical and practical difficulties of developing a tumouristatic drug in the treatment of cancer.
AU Lynch K.
CS Dr. K. Lynch, Medical Department, Novartis Pharmaceuticals Pty. Ltd., 54 Waterloo Road, North Ryde, NSW 2113, Australia
SO International Journal of Pharmaceutical Medicine, (1999) 13/3 (127-136). Refs: 104
ISSN: 1364-9027 CODEN: IJPMFV
CY United Kingdom
DT Journal; Article
FS 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB The processes of tumour growth, invasion and metastatic spread are dependent on the remodelling of extracellular matrix (ECM) and formation of new blood vessels (angiogenesis). There is now widespread conviction that inhibitors of ECM remodelling and angiogenesis will offer a mechanism to control primary tumour growth and prevent the spread of metastases. The matrix metalloproteinases (MMPs) are a family of enzymes that play a crucial role in these processes, and their inhibition represents a promising target for drug development. Development of candidate inhibitors of MMP drugs is, however, problematic. The compound should ideally be suitable for long-term, oral administration. Since the drugs are anticipated to be cytostatic rather than cytotoxic, conventional measures of tumour regression in early clinical trials are inappropriate. Instead, reliance may be made on models of animal cancer and the use of surrogate markers of disease progression for the design of pivotal phase III studies. In the later phase trials, selection of dose, interpretation of concentration-effect relationships and the description of novel toxicity profiles are only part of the development challenge. This paper discusses the theoretical and practical difficulties of developing a tumouristatic drug in the treatment of cancer, with particular emphasis on the MMP inhibitor marimastat.
CT Medical Descriptors:
drug development
tumor growth: ET, etiology
cancer invasion: ET, etiology
metastasis: ET, etiology
extracellular matrix
tumor vascularization: ET, etiology
angiogenesis
cytostasis
cancer inhibition
drug dose
concentration response
drug synthesis
drug blood level
cancer: DT, drug therapy
polyarthritis: SI, side effect
arthralgia: SI, side effect
myalgia: SI, side effect
tendinitis: SI, side effect

human
nonhuman
animal experiment
animal model
oral drug administration
clinical trial
meta analysis
article
priority journal
Drug Descriptors:
*matrix metalloproteinase inhibitor: AE, adverse drug reaction
*matrix metalloproteinase inhibitor: CT, clinical trial
*matrix metalloproteinase inhibitor: CB, drug combination
*matrix metalloproteinase inhibitor: DV, drug development
*matrix metalloproteinase inhibitor: DO, drug dose
*matrix metalloproteinase inhibitor: DT, drug therapy
*matrix metalloproteinase inhibitor: PK, pharmacokinetics
matrix metalloproteinase: EC, endogenous compound
cytostatic agent: AE, adverse drug reaction
cytostatic agent: CT, clinical trial
cytostatic agent: DV, drug development
cytostatic agent: DO, drug dose
cytostatic agent: DT, drug therapy
cytostatic agent: PK, pharmacokinetics
marimastat: AE, adverse drug reaction
marimastat: CT, clinical trial
marimastat: DV, drug development
marimastat: DO, drug dose
marimastat: DT, drug therapy
cgs 27023a: DV, drug development
3 cyclopentylmethyl 2 [(3,3,4 trimethyl 2,5 dioxo 1 imidazolidinyl)methyl] 4 oxo 4 piperidinobutyrohydroxamic acid: DV, drug development
sc 44463: DV, drug development
ilomastat: CT, clinical trial
ilomastat: DT, drug therapy
batimastat: CT, clinical trial
batimastat: DT, drug therapy
RN (marimastat) 154039-60-8; (cgs 27023a) 169799-04-6; (3 cyclopentylmethyl 2 [(3,3,4 trimethyl 2,5 dioxo 1 imidazolidinyl)methyl] 4 oxo 4 piperidinobutyrohydroxamic acid) 190648-49-8; (ilomastat) **142880-36-2**; (batimastat) 130370-60-4, 130464-84-5
CN (1) Ro 32 3555; (2) Cgs 27023a; (3) Sc 44463; Gm 6001
CO (1) Hoffmann La Roche; (2) Ciba Geigy; (3) Searle

L59 ANSWER 20 OF 25 EMBASE
on STN
AN 1999263317 EMBASE
TI Design and synthetic considerations of matrix metalloproteinase inhibitors.
AU Skotnicki J.S.; Zask A.; Nelson F.C.; Albright J.D.; Levin J.I.
CS J.S. Skotnicki, Chemical Sciences, Wyeth-Ayerst Research, Pearl River, NY 10965, United States. skotnij@war.wyeth.com
SO Annals of the New York Academy of Sciences, (1999) 878/- (61-72).
Refs: 35
ISSN: 0077-8923 CODEN: ANYAA
CY United States
DT Journal; Conference Article
FS 029 Clinical Biochemistry
030 Pharmacology

037 Drug Literature Index
LA English
SL English
AB Experimental evidence confirms that the matrix metalloproteinases (MMPs) play a fundamental role in a wide variety of pathologic con- ditions that involve connective tissue destruction including osteoarthritis and rheumatoid arthritis, tumor metastasis and angiogenesis, corneal ulceration, multiple sclerosis, periodontal disease, and atherosclerosis. Modulation of MMP regulation is possible at several biochemical sites, but direct inhibition of enzyme action provides a particularly attractive target for therapeutic intervention. Hypotheses concerning inhibition of specific MMP(s) with respect to disease target and/or side-effect profile have emerged. Examples are presented of recent advances in medicinal chemistry approaches to the design of matrix metalloproteinase inhibitors (MMPIs), approaches that address structural requirements and that influence potency, selectivity, and bioavailability. Two important approaches to the design, synthesis, and biological evaluation of MMPIs are highlighted: (1) the invention of alternatives to hydroxamic acid zinc chelators and (2) the construction of nonpeptide scaffolds. One current example in each of these two approaches from our own work is described.
CT Medical Descriptors:
drug design
drug synthesis
connective tissue disease: ET, etiology
osteoarthritis: ET, etiology
rheumatoid arthritis: ET, etiology
metastasis: ET, etiology
tumor vascularization: ET, etiology
cornea ulcer: ET, etiology
multiple sclerosis: ET, etiology
periodontal disease: ET, etiology
atherosclerosis: ET, etiology
enzyme regulation
enzyme inhibition
drug structure
drug potency
drug selectivity
drug bioavailability
conference paper
Drug Descriptors:
*matrix metalloproteinase inhibitor: AN, drug analysis
*matrix metalloproteinase inhibitor: DV, drug development
*matrix metalloproteinase inhibitor: PK, pharmacokinetics
matrix metalloproteinase: EC, endogenous compound
hydroxamic acid: DV, drug development
chelating agent: DV, drug development
cgs 27023a: AN, drug analysis
cgs 27023a: DV, drug development
ct 1746: AN, drug analysis
ct 1746: DV, drug development
ilomastat: AN, drug analysis
ilomastat: DV, drug development
marimastat: AN, drug analysis
marimastat: DV, drug development
ag 3340: AN, drug analysis
ag 3340: DV, drug development
3 cyclopentylmethyl 2 [(3,3,4 trimethyl 2,5 dioxo 1 imidazolidinyl)methyl] 4 oxo 4 piperidinobutyrohydroxamic acid: AN, drug analysis
3 cyclopentylmethyl 2 [(3,3,4 trimethyl 2,5 dioxo 1 imidazolidinyl)methyl]

4 oxo 4 piperidinobutyrohydroxamic acid: DV, drug development
trocade: AN, drug analysis
trocade: DV, drug development
rs 130830: AN, drug analysis
rs 130830: DV, drug development
4 [4,4 (chlorophenyl)phenyl] 4 oxo (phenylthiomethyl)butanoic acid: AN, drug analysis
4 [4,4 (chlorophenyl)phenyl] 4 oxo (phenylthiomethyl)butanoic acid: DV, drug development
doxycycline: AN, drug analysis
doxycycline: DV, drug development

RN (cgs 27023a) 169799-04-6; (ilomastat) **142880-36-2**; (marimastat) 154039-60-8; (ag 3340) 195008-93-6; (3 cyclopentylmethyl 2 [(3,3,4 trimethyl 2,5 dioxo 1 imidazolidinyl)methyl] 4 oxo 4 piperidinobutyrohydroxamic acid) 190648-49-8; (doxycycline) 10592-13-9, 17086-28-1, 564-25-0

CN Ct 1746; Gm 6001; Bb 2516; Ro 32 3555; Trocade; Rs 130830; Bay 12 9566; Periostat

CO Merck; Glaxo; Pfizer; British Biotechnology; Agouron; Celltech; Chiroscience; Smith Kline Beecham; Wyeth Ayerst; Hoffmann La Roche; Novartis; Ono; Shionogi; Warner Lambert; Hoechst; Monsanto; Rhone Poulenc Rorer; Bayer; Abbott; Ciba Geigy

L59 ANSWER 21 OF 25 EMBASE on STN

AN 97126684 EMBASE

DN 1997126684

TI Tumor-associated angiogenesis: Mechanisms, clinical implications, and therapeutic strategies.

AU Pluda J.M.

CS Dr. J.M. Pluda, Investigational Drug Branch, CTEP DCTDC, NCI, 6130 Executive Blvd, Rockville, MD 20852, United States

SO Seminars in Oncology, (1997) 24/2 (203-218).
Refs: 181
ISSN: 0093-7754 CODEN: SOLGAV

CY United States

DT Journal; Conference Article

FS 016 Cancer
037 Drug Literature Index

LA English

SL English

AB Compelling data implicate angiogenesis and tumor-associated neovascularization as a central pathogenic step in the process of tumor growth, invasion, and metastasis. These complex processes involve multiple steps and pathways dependent on the local balance between positive and negative regulatory factors, as well as interactions among the tumor, its vasculature, and the surrounding extracellular tissue matrix. A tumor remains in a dormant state, the cellular proliferation rate balanced by the apoptotic rate, unable to grow in size beyond a few millimeters in the absence of the acquired angiogenic phenotype. The mechanism by which tumors switch to the angiogenic phenotype is unknown. Therapeutic agents and strategies are being devised either to interrupt or inhibit one or more of the pathogenic steps involved in the process of tumor neovascularization or to directly target and destroy the tumor vasculature. Therapies affecting an end target or pathway that cannot be circumvented by alternate mechanisms may significantly enhance efficacy and broaden applicability. These approaches may result in small, avascular tumors maintained in a dormant state or, perhaps in combination with cytotoxic therapies, they may potentiate shrinkage of tumors to, and

maintain them, in a dormant state. As more powerful antiangiogenic agents are developed, perhaps even these dormant microscopic loci may be eradicated. Antiangiogenesis agents and strategies differ from the usual cancer therapeutic approaches; therefore, investigators must devise new paradigms for the clinical development of agents that may only have a static effect on tumors and require prolonged, chronic administration. Methods to assess the in viva biologic activity of these compounds in patients are needed. Ultimately, antiangiogenic therapy may provide an additional novel cancer treatment suitable for combination with standard therapies.

CT Medical Descriptors:
*angiogenesis
*cancer growth
*metastasis potential
cancer inhibition
cancer invasion
carcinogenesis
clinical trial
conference paper
drug effect
human
nonhuman
priority journal
tumor regression
tumor vascularization
Drug Descriptors:
*ag 3340: DV, drug development
*ag 3340: PD, pharmacology
*angiogenesis inhibitor: PD, pharmacology
*angiogenesis inhibitor: DV, drug development
*cm 101: CT, clinical trial
*cm 101: PD, pharmacology
*ct 2584: PD, pharmacology
*ct 2584: CT, clinical trial
*marimastat: PD, pharmacology
*marimastat: CT, clinical trial
*vitaxin: DV, drug development
*vitaxin: PD, pharmacology
angiostatin: PD, pharmacology
angiostatin: DV, drug development
batimastat: PD, pharmacology
batimastat: CT, clinical trial
col 3
fumagillol chloroacetylcarbamate: PD, pharmacology
fumagillol chloroacetylcarbamate: CT, clinical trial
ilomastat: PD, pharmacology
ilomastat: DV, drug development
interleukin 12: PD, pharmacology
interleukin 12: CT, clinical trial
metastat: DV, drug development
metastat: PD, pharmacology
pentosan polysulfate: PD, pharmacology
pentosan polysulfate: CT, clinical trial
tecogalan: CT, clinical trial
tecogalan: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: PD, pharmacology
unclassified drug
RN (marimastat) 154039-60-8; (angiostatin) 172642-30-7, 86090-08-6;

(batimastat) 130370-60-4, 130464-84-5; (fumagillol chloroacetylcarbamate) 129298-91-5; (ilomastat) **142880-36-2**; (interleukin 12) 138415-13-1; (pentosan polysulfate) 116001-96-8, 37300-21-3, 37319-17-8; (tecogalan) 134633-29-7; (thalidomide) 50-35-1

CN Agm 1470; Ds 4152; Bb 94; Bb 2516; Col 3

L59 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:978677 HCAPLUS
DN 124:30411
ED Entered STN: 13 Dec 1995
TI Tryptophan derivatives as synthetic matrix metalloprotease inhibitors and uses thereof
IN Levy, Daniel E.; Grobelny, Damian; Tang, Peng Cho; Holme, Kevin R.; Galardy, Richard E.; Schultz, Gregory S.; Nematalla, Assad; Musser, John H.
PA Glycomed Incorp., USA
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C07D209-20
ICS A61K031-405
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 7
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9519965	A1	19950727	WO 1995-US783	19950120
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5892112	A	19990406	US 1994-184727	19940121
	AU 9516049	A1	19950808	AU 1995-16049	19950120
	EP 690841	A1	19960110	EP 1995-908086	19950120
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09501183	T2	19970204	JP 1995-519668	19950120
PRAI	US 1994-184727	A	19940121		
	US 1990-616021	A1	19901120		
	US 1990-615798	A2	19901121		
	US 1991-747751	A1	19910820		
	US 1991-747752	A2	19910820		
	US 1992-817039	A2	19920107		
	US 1992-881630	A1	19920512		
	US 1993-44324	A2	19930407		
	WO 1995-US783	W	19950120		

OS CASREACT 124:30411; MARPAT 124:30411
AB Synthetic mammalian matrix metalloprotease inhibitors are disclosed, that are useful for treating or preventing diseases including skin disorders, keratoconus, restenosis, rheumatoid arthritis, wounds, cancer, angiogenesis and shock. The compds. include those of general formula R7ON(R6)CO(CHR1)nCH(R2)CON(R3)CH(R4)COX [where R1 = H, alkyl; R2 = H, alkyl, NHZ; Z = alkyl, alkanoyl, alkoxycarbonyl; or R1R2 = (CH2)3-5; R3 = H, alkyl; R4 = fused or conjugated (un)substituted bicycloarylmethylene; n = 0-2; X = OH, alkoxy, amino, alkylamino, amino acid or amide; R6 = H, alkyl; R7 = H, alkyl, acyl; amide group CONR3 may be replaced by selected isosteric groups]. For example, benzyl 4-methyl-2-oxopentanoate underwent Wittig reaction with Ph3P:CHCO2Me (100%), hydrogenation of the formed unsatd. diester (86%), peptide coupling of the obtained monoacid with H-Trp-NHMe.HCl and separation of diastereomers (83%), and reaction with NH2OH (56% and 72%), to give title compds. D,L- and L,L-HONHCOCH2CH(Bu-iso)CO-

Trp-NHMe (I). In the phorbol ester-induced epidermal hyperplasia mouse model, D,L-I reduced ear thickness from 229% of control to only 140% of control. Over 40 synthetic examples are given, plus enzyme assays, and addnl. biol. tests showing activity against angiogenesis, chronic dermal wounds, peritonitis, metastasis, hypovolemic shock, and restenosis.

ST tryptophan matrix metalloprotease inhibitor prepn

IT Blood vessel
(**angiogenesis** inhibition; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Wound healing promoters
(preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Psoriasis
Shock
Skin, disease
(treatment; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Inflammation inhibitors
(antiarthritics, preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Skin, disease
(hyperplasia, treatment; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Eye, disease
(keratoconus, treatment; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Neoplasm inhibitors
(metastasis, preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT Heart, disease
(restenosis, treatment; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT 9001-12-1, Collagenase 79955-99-0, Stromelysin 146480-35-5, Gelatinase A 146480-36-6, Gelatinase B
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT 1676-74-0P 5702-99-8P 14035-83-7P, Isobutylsuccinic anhydride
18908-20-8P 66095-18-9P 96136-13-9P 111955-05-6P 132631-36-8P,
2-Isobutyl-3-(methoxycarbonyl)propionic acid 142880-30-6P 142880-31-7P
142880-33-9P 142880-34-0P 142880-35-1P 142880-39-5P 142880-48-6P
142880-49-7P 142880-51-1P 142880-52-2P 142880-61-3P 142880-63-5P
142880-64-6P 142880-65-7P 142880-76-0P 142902-75-8P 143985-45-9P
143985-46-0P 143985-47-1P 143985-48-2P 143985-49-3P 143985-50-6P
144070-02-0P 144070-04-2P 162550-03-0P 166247-21-8P 171347-86-7P
171347-87-8P 171347-88-9P 171347-89-0P 171347-90-3P 171347-91-4P
171347-92-5P 171347-94-7P 171347-95-8P 171347-96-9P 171347-97-0P
171347-98-1P 171347-99-2P 171348-00-8P **171348-01-9P**
171348-02-0P 171348-03-1P 171348-04-2P
171348-05-3P 171348-06-4P 171348-07-5P 171348-08-6P 171348-09-7P
171348-10-0P, L-Tryptophan (4-pyridylmethyl)amide 171348-13-3P
171483-46-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT **142880-36-2P 142880-37-3P 142880-40-8P**
142880-42-0P **142880-46-4P** 142880-54-4P **142880-59-9P**
142880-60-2P 142880-62-4P 142880-68-0P 142880-72-6P

142880-73-7P 142880-74-8P **142902-71-4P** 142902-72-5P
143985-23-3P **144007-87-4P** 144069-99-8P 144070-00-8P
144070-05-3P 144070-06-4P **159686-32-5P** **159686-33-6P**
159686-34-7P **162550-05-2P** 171347-73-2P 171347-74-3P
171347-75-4P 171347-76-5P 171347-77-6P 171347-78-7P
171347-79-8P **171347-80-1P** **171347-81-2P**
171347-82-3P **171347-83-4P** **171347-84-5P**
171347-85-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT 141907-41-7, Matrix metalloproteinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

IT 65-85-0, Benzoic acid, reactions 73-22-3, L-Tryptophan, reactions 74-89-5, Methanamine, reactions 75-44-5, Carbonic dichloride 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 108-31-6, 2,5-Furandione, reactions 108-91-8, Cyclohexylamine, reactions 115-11-7, reactions 123-00-2, 3-(4-Morpholinyl)propylamine 124-09-4, 1,6-Hexanediamine, reactions 459-46-1, p-Fluorobenzyl bromide 501-53-1, Benzyl chloroformate 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 2627-86-3, (S)-Methylbenzylamine 2687-43-6, O-Benzylhydroxylamine hydrochloride 3731-53-1, 4-(Aminomethyl)pyridine 4502-00-5 5437-45-6, Bromoacetic acid benzyl ester 13139-14-5 13149-00-3, cis-1,2-Cyclohexanedicarboxylic anhydride 14035-83-7, Isobutylsuccinic anhydride 14166-21-3, trans-1,2-Cyclohexanedicarboxylic anhydride 35858-81-2, L-Tryptophan benzyl ester hydrochloride 53064-79-2, Iodomethyl pivalate 69621-45-0, L-Tryptophanylglycine methyl ester 111372-25-9, L-Tryptophan dodecylamide 112245-04-2 119893-56-0 132631-36-8 142880-44-2 142880-45-3 142880-55-5, L-Tryptophan piperidinamide 142902-74-7 171348-11-1 171348-12-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of tryptophan derivs. as matrix metalloprotease inhibitors)

L59 ANSWER 23 OF 25 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95144883 EMBASE
DN 1995144883
TI Recent progress in the development of anti-tumor metastatic drugs.
AU Kumagai H.
CS Research Center, Asahi Glass Co., Ltd., 1150 Hazawa-cho,Kanagawa-ku, Yokohama 221, Japan
SO Japanese Journal of Cancer and Chemotherapy, (1995) 22/5 (585-591). ISSN: 0385-0684 CODEN: GTKRDX
CY Japan
DT Journal; General Review
FS 016 Cancer
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LA Japanese
SL Japanese; English
AB Metastasis is often a terminal stage of cancer when tumor fragments lodge and grow in different parts of the body. There is currently no way to prevent metastasis, and there are few effective treatments. We believe

that it is very important to develop an anti-tumor metastatic drug. Recent studies on the mechanism of tumor metastasis reveal that this multi-step process requires complex interaction between the tumor cells and their environment. In vitro experiments and animal cancer model studies have shown that the inhibitors of invasion (including adhesion, proteolysis, and migration) and neovascularization may suppress tumor metastasis. The author shows the mechanism of tumor metastasis, an in vitro screening method, and the recent progress of the development of various candidate anti-tumor metastatic drugs, including invasion inhibiting factor-2. Finally, the importance of the development of an anti-tumor metastatic drug in Japan is underscored.

CT Medical Descriptors:
*metastasis
cell adhesion
cell migration
neovascularization (pathology)
nonhuman
protein degradation
review
screening
Drug Descriptors:
*antineoplastic agent: PD, pharmacology
*antineoplastic agent: DV, drug development
angiostatin: DV, drug development
angiostatin: PD, pharmacology
batimastat: PD, pharmacology
batimastat: DV, drug development
carboxyamidotriazole: PD, pharmacology
carboxyamidotriazole: DV, drug development
disintegrin: DV, drug development
disintegrin: PD, pharmacology
fumagillol chloroacetylcarbamate: DV, drug development
fumagillol chloroacetylcarbamate: PD, pharmacology
ilomastat: PD, pharmacology
ilomastat: DV, drug development
invasion inhibiting factor 2: DV, drug development
invasion inhibiting factor 2: PD, pharmacology
recombinant thrombocyte factor 4: PD, pharmacology
recombinant thrombocyte factor 4: DV, drug development
superoxide dismutase: DV, drug development
superoxide dismutase: PD, pharmacology
tecogalan: PD, pharmacology
tecogalan: DV, drug development
verapamil: PD, pharmacology
verapamil: DV, drug development
unclassified drug

RN (angiostatin) 172642-30-7, 86090-08-6; (batimastat) 130370-60-4, 130464-84-5; (fumagillol chloroacetylcarbamate) 129298-91-5; (ilomastat) **142880-36-2**; (superoxide dismutase) 37294-21-6, 9016-01-7, 9054-89-1; (tecogalan) 134633-29-7; (verapamil) 152-11-4, 52-53-9

CN Tnp 470; Ds 4152

L59 ANSWER 24 OF 25 EMBASE
on STN

AN 94283412 EMBASE

DN 1994283412

TI Inhibition of angiogenesis by the matrix metalloprotease inhibitor N-[2R-2-(hydroxamidocarbonymethyl)-4-methylpentanoyl)]-L-tryptophan methylamide.

AU Galardy R.E.; Grobelny D.; Foellmer H.G.; Fernandez L.A.

CS Glycomed, Inc., 860 Atlantic Ave.,Alameda, CA 94501, United States
SO Cancer Research, (1994) 54/17 (4715-4718).
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 012 Ophthalmology
016 Cancer
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The inhibitor N-[2R-2-(hydroxamidocarbonymethyl)-4-methylpentanoyl)]-L-tryptophan methylamide specifically blocks several matrix metalloproteases, enzymes which are thought to be involved in angiogenesis. An extract of Walker 256 carcinoma in Hydron pellets implanted in the corneas of Sprague- Dawley rats was used to stimulate angiogenesis from the vessels of the limbus. Angiogenesis was graded visually as the distance penetrated into the cornea and the number of vessels generated. The vessel area was also measured by image analysis using Image 1 software. Continuous i.v. administration of N-[2-(hydroxamidocarbonymethyl)-4-methylpentanoyl)]-L-tryptophan methylamide at 32 mg/kg/day (n = 17) via syringe pump reduced vessel number [25.06 ± 5.9 (SEM) compared to 65.33 ± 9.0] and vessel area (26.14 ± 3.2 mm2 compared with 40.96 ± 4.6 mm2), but not distance penetrated, compared to vehicle- treated control eyes after 6 days. These results confirm the suspected role for matrix metalloproteases in angiogenesis and suggest that inhibitors of these enzymes may be angiostatic agents.
CT Medical Descriptors:
*angiogenesis
*cornea perforation
***neovascularization (pathology)**
animal experiment
animal model
article
controlled study
dose response
drug megadose
enzyme inhibition
image analysis
intravenous drug administration
nonhuman
priority journal
rat
walker carcinoma
Drug Descriptors:
*collagenase: EC, endogenous compound
*dimethyl sulfoxide
*metalloproteinase inhibitor: DO, drug dose
*metalloproteinase inhibitor: PD, pharmacology
*polymacon
ilomastat: DO, drug dose
ilomastat: PD, pharmacology
RN (collagenase) 9001-12-1; (dimethyl sulfoxide) 67-68-5; (polymacon) 25053-81-0, 25249-16-5, 98932-78-6; (ilomastat) **142880-36-2**
CN Gm 6001

L59 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:245779 HCAPLUS

DN 120:245779
ED Entered STN: 14 May 1994
TI Inhibition of **angiogenesis** by synthetic matrix metalloprotease inhibitors
IN Galardy, Richard E.
PA Glycomed, Inc., USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9313741	A2	19930722	WO 1993-US54	19930104
	WO 9313741	A3	19930819		
	W: AU, CA, DK, JP, NO				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5268384	A	19931207	US 1992-817039	19920107
	AU 9334332	A1	19930803	AU 1993-34332	19930104
	JP 07503007	T2	19950330	JP 1993-512526	19930104
	EP 663823	A1	19950726	EP 1993-902938	19930104
	EP 663823	B1	20001122		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 197667	E	20001215	AT 1993-902938	19930104
PRAI	US 1992-817039	A	19920107		
	US 1990-615798	A2	19901121		
	US 1991-747751	A2	19910820		
	US 1991-747752	A2	19910820		
	WO 1993-US54	A	19930104		

OS MARPAT 120:245779
AB Peptides R7ONR6CO[CHR1]nCHR2CONR3CHR4COR5 [R1 = H, alkyl; R2 = alkyl; R1R2 = alkylene; R3 = H, alkyl; R4 = fused or conjugated (un)substituted bicycloarylmethyl; R5 = (un)substituted OH, NH2, amino acid residue; R6 = H, alkyl; R7 = H, alkyl, acyl; n = 0-2] were prepared as angiogenesis and metalloproteinase inhibitors. Thus, HONHCOCH2CH(CH2CHMe2)CO-L-Trp-NHMe (I) was prepared as a mixture of diastereomers from Me2CHCH2COCO2Na via reaction with Ph3P:CHCO2Me and H-Trp-NHMe.HCl. The isomers had matrix metalloproteinase-inhibiting Ki of 10 and 150 nM, resp.
ST hydroxylaminocarbonylalkanoyltryptophanamide prepn metalloproteinase inhibitor; tryptophanamide hydroxylaminocarbonylalkanoyl prepn metalloproteinase inhibitor
IT **Blood vessel, disease**
(**neovascularization**, inhibitors, hydroxylaminocarbonylalkanoyltryptophanamides)
IT 81669-70-7, Metalloproteinase
RL: USES (Uses)
(inhibitors, hydroxylaminocarbonylalkanoyltryptophanamides)
IT 13658-97-4P 66095-18-9P 96136-13-9P 111955-05-6P 132631-36-8P
142880-30-6P 142880-31-7P 142880-34-0P 142880-35-1P 142880-39-5P
142880-49-7P 142880-51-1P 142880-52-2P 142880-63-5P 142880-64-6P
142880-65-7P 142902-75-8P 143985-45-9P 143985-47-1P 143985-48-2P
143985-49-3P 143985-50-6P **143985-51-7P** 144070-02-0P
144070-03-1P 144070-04-2P 152993-10-7P 152993-11-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate in preparation of metalloproteinase inhibiting hydroxylaminocarbonylalkanoyltryptophanamides)

IT **142880-36-2P 142880-37-3P 142880-38-4P**
142880-53-3P 142880-54-4P **142880-58-8P**
142880-62-4P 142880-66-8P 142880-69-1P 142880-72-6P
142880-73-7P 142880-74-8P 142902-72-5P **143985-20-0P**
143985-21-1P **143985-22-2P 144069-98-7P** 144069-99-8P
144070-00-8P 144070-01-9P 144070-05-3P 144070-06-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and metalloproteinase inhibiting activity of)

IT 142880-48-6P **142880-53-3P 142880-75-9P** 152993-12-9P
152993-13-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 124-09-4, 1,6-Hexanediamine, reactions 2605-67-6, Methyl triphenylphosphoranylideneacetate 4502-00-5 13149-00-3, cis-1,2-Cyclohexanedicarboxylic anhydride 14166-21-3 69621-45-0 111372-25-9, L-Tryptophan dodecylamide 119893-56-0 142880-33-9 142880-44-2 142880-45-3 142880-47-5 142880-55-5, L-Tryptophan piperidinamide 142902-74-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant, in preparation of metalloproteinase inhibiting hydroxylaminocarbonylalkanoyltryptophanamides)

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